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ACUTE PULMONARY ŒDEMA*

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ACUTE PULMONARY ŒDEMA is a medical emergency as well known to the physician as it is poorly understood. Only occasionally in recent years have the more widely read Journals considered this subject,[1] with the result that many clinicians are unaware of recent interesting and valuable investigative work on the subject. As most of these studies are concerned with pathogenesis and/or treatment these aspects of the problem are most informative to consider.

Recorded knowledge of acute pulmonary œdema has been accumulating for two hundred years, since Maloët's clinical description in 1752.[2] It has become apparent that this syndrome occurs in a bewildering variety of clinical states. This led to investigations, the best known of which are those of Welch,[3] 1878, Lian[4] 1910 and Vaquez[5] 1913 which resulted in the well known theory of pulmonary œdema as a consequence of left ventricular failure. German[6] and Italian[7] workers soon challenged this concept and in review of their work Luisada[7] in 1940 stated, "as experimental and clinical observations on pulmonary œdema have accumulated, it has become clear that the validity of the 'back pressure' or 'left ventricle failure' theory of acute pulmonary œdema can no longer be considered as established." The so-called neurogenic theory is becoming more widely accepted by most workers in the field as the still incompletely understood but probably true mechanism of acute pulmonary œdema. Clinicians almost universally, while adhering in thought to the left ventricular failure theory, apply the teachings of the neurogenic theory in their use of morphine as the therapeutic agent of choice.

Acute pulmonary œdema, regardless of cause, is characterized by transudation of blood serum from pulmonary capillaries to alveolar spaces. There are many clinical and experimental situations in which this syndrome develops, but our discussion of pathogenesis will be restricted to the basic anatomical and physiological factors involved in the formation of alveolar transudate. Proceeding from lips to pharynx, to bronchi and alveoli and beyond into alveolar capillaries, pulmonary and systemic blood-vessels and their controlling nerves, we shall discuss briefly the principles whereby so many situations result in a single manifestation—acute pulmonary œdema.

Intra-pleural pressure, ranging between –2.5 mm. Hg. in quiet expiration and –6 mm. in inspiration can be increased more than five-fold in forceful respiration,[8] thus aspirating blood into the intra-thoracic vessels and creating a situation favourable to transudation. Yamada[9] demonstrated the development of pleural effusions under such negative pressures during physical exertion. The alteration suddenly of intra-bronchial pressure relationship by tracheotomy in long-standing laryngeal obstructions has resulted in pulmonary œdema.[10a] In such cases, while a high negative pressure in inspiration is corrected, the beneficial effects to be considered later of a high positive pressure in expiration are simultaneously negated. Inspiration through a narrowed air-way is believed to be one of the factors leading to pulmonary œdema in asthma;[10a] in which case the bronchial muscle is implicated.

Even more distally in the tracheo-bronchial tree the air-way can, of course, be narrowed to produce high inspiratory negative pressure in the alveoli as a result of inflammatory swelling of the mucosa, due either to organisms or chemicals.

The terminal air-containing structure, the alveolus, is as the primary site of occurrence of acute œdema worthy of considerable comment. At this point, barometric pressure exerts its

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aggravating effect by aspirating tissue fluids through the single cell layer of the alveolar wall when pressure is negative because of mechanisms already mentioned. The converse beneficial effect of reducing transudation by positive pressure respiration was demonstrated in the case of gas poisoning by Norton[11] in 1897. Animal experiments led Haven Emerson[12] to recommend the technique to clinicians again in 1909, and its successful application was recorded the same year.[13] Barach[10b, 14, 15] has repeatedly advocated the use of positive pressure and with Eckman[10c] developed a very satisfactory mask for the purpose. An occluding diaphragm equipped with five openings, graduated in size so as to provide resistance varying from zero to plus 4 cm. of water, is placed over the expiratory flutter valve of a tightly fitting face mask provided with a 2 litre reservoir bag from which inspiration is freely made at atmospheric or slightly positive pressure. This reservoir can be filled by continuous flow with any concentration of oxygen in air desired by the addition of an injector meter between supply tank and mask tubing.

Partial pressure of oxygen is important, as hypoxia increases the permeability of the membrane to transudate.[10d, 16a] Several authors[10d, 17] made the observation that it is not tissue fluid in the alveoli that endangers life, but the hypoxia that develops when the tissue fluid mixes with air and mucus in the bronchioles and bronchi to form a froth. Luisada[17] has significantly reduced mortality in experimental animals by the use of anti-frothing agents in vapour form in the inspired air, ethyl alcohol being the most satisfactory substance studied.

Probably the most important single structure concerned in the development of acute pulmonary œdema is the alveolar capillary. As Drinker[16b] points out its estimated hydrostatic pressure of 10 mm. is considerably less than the opposed colloid osmotic pressure of 25 to 30 mm. mercury and this can, in fact, result in the absorption of water or saline solution from the alveolar space. This favourable situation can be entirely reversed by a change in capillary permeability occurring in acute inflammation from whatever cause. Phosgene gas,[14] for example, being relatively poorly soluble in water does not dissolve in the moisture on bronchial walls to produce immediate warning inflammation there. Rather, it penetrates to the alveoli and so causes a delayed diffuse inflammation, whereupon transudate pours freely into the alveoli, froths in the bronchioles and asphyxiates the patient. Anoxia is considered to alter capillary permeability in all bodily situations, including the lungs. Many authors maintain that reflex influences can produce like changes, all of which factors result in transudation in acute pulmonary œdema.

A rarely considered protective mechanism incorporated in the lung structure has been brought to attention, after years of work, in a recent monograph by Drinker.[16] By one of several experimental methods producing acute pulmonary œdema in dogs he has observed that there is a marked increase in right lymphatic duct flow which might well combat the development of alveolar transudation, were it not that the lymph duct is a relatively narrow structure and is thus incapable of handling large amounts of fluid arriving from many areas of the lung field at once.

The commonly acceptable clinical explanation of acute pulmonary œdema as a failure of the left ventricle output, with resultant increased pulmonary capillary pressure and transudation under the filling force of a competent right ventricle, fails to explain many experimental and clinical cases of this syndrome.[7] Cataldi, by damaging the right ventricle with silver nitrate injections, could produce pulmonary œdema in right ventricle failure. The experiments upon which the concept was based[1] were extremely mutilating and produced other changes, such as cerebral anoxia and intense autonomic nervous stimulation, in themselves now known to produce acute pulmonary œdema.

The functional reserve of the lungs as to alveolar membrane area and capillary network is very large[1] and it is probable that here, as in other vital organs, only a small percentage of the capillaries are functioning at any one time. The blood volume in the lungs varies widely, and is probably under sympathetic vasomotor control of the peripheral circulation rather than of the pulmonary circulation.[19] Sarnoff has shown in animals by vascular catheterization techniques a marked rise in pulmonary venous pressure in the presence of vasoconstrictor states. Several experimental methods of œdema production depend on a preliminary increase in blood volume by massive infusion of intravenous saline to destroy this functional reserve and we have seen acute pulmonary œdema develop

clinically following rapid infusion of 1,000 c.c. glucose-saline. Conversely, it is of value to recall Ebert and Stead's[21] quantitative evaluation of the well known therapeutic measure of tourniquet applications to the extremities. For example, 15% of their total blood volume was removed from the head, trunk and arm by placing venous tourniquets at diastolic pressures on three extremities, which is as much blood as removed by a 700 c.c. phlebotomy.

Discussion of total or fractional blood volume changes leads to consideration of compensatory reflex mechanisms. Among the best known are the distension reflex of Bainbridge,[8b] whereby overfilling of the right auricle leads to tachycardia and increased cardiac output with reduction of the intrathoracic venous pressure. The aortic stretch reflexes and carotid sinus reflexes[8c] act, as is well known, in the opposite direction to produce bradycardia and decreased output with lowering of blood pressure when aortic or carotid pressures become excessive. These two latter reflexes both tend, therefore, to the production of pulmonary transudate. Many cases of acute pulmonary œdema have been described, occurring in the presence of intracranial irritation from concussion, fracture or hæmorrhage clinically, and increased intracranial vascular pressure,[7] anoxia,[7] fibrin irritation[1] or electrical stimulation experimentally. Interruption of these reflex arcs by sympathetic section has given protection against development of acute pulmonary œdema in the hands of Luisada and others.[23] Various sympatholytic drugs have been shown to be effective by several authors.[24, 25, 26] In the opinions of many workers[7] in the field, there are also pulmonary reflexes which alter permeability of alveolar capillaries; it is hard to explain otherwise the fact, demonstrated by Cameron and Cheng,[1] that the most diverse causes of acute pulmonary œdema result in production of similar transudates high in protein. It is equally difficult to explain those clinical cases where pulmonary œdema can be induced or cleared by psychiatric methods.

TREATMENT

It should now be apparent that no single factor is liable to be wholly causative of an attack of acute pulmonary œdema. We can turn to discussion of treatment with the attitude that rational therapy must, of necessity, be multiple and based on analysis of the pathological physiology involved in the case under treatment.

The patient's insistent tendency to sit upright is to be encouraged. Venous return is reduced by gravity, particularly if the feet are allowed to hang down, and even more so if the old European custom of placing the feet in hot water[27] is followed so as to increase pooling of blood in the legs. Considering possible adverse effects, one must remember that the diaphragms are free of the weight of abdominal viscera and, by increased amplitude and rate of excursion, can aspirate blood into the lung fields, to increase negative intra-pleural and intra-alveolar pressure, favouring transudate. Furthermore, in cases with low cardiac output, such as acute myocardial infarction, the upright posture tends to increase the degree of cerebral anoxia with consequent reflex intensification of œdema.

The marked effectiveness of morphine is certainly not due to any effect of this drug on left ventricular failure, but can very well be due to reduction of central nervous system activity with resultant decrease of nervous stimuli to the vascular system.[7] Phlebotomy also reduces return but can disadvantageously lower oxygen carrying capacity by hæmoglobin depletion and blood osmotic pressure by plasma depletion, if this method is used repeatedly. Extremity tourniquets can obtain the same beneficial effect without these shortcomings.

Oxygen, while it can theoretically lessen reflex factors by better oxygenation of the nerve tissue, is to be expected to be useless if prevented from reaching the alveolar membrane by the froth of fully developed acute pulmonary œdema. Therefore, if it is to be effective, it must be used before the clinical syndrome is obvious.[16c] While animal experimentation indicates that 100% oxygen is toxic and can produce pulmonary œdema, it has been demonstrated clinically that the interruptions necessitated by feedings and attention to oral hygiene in the human, permits use of such concentrations for up to two weeks with entire safety.[10c]

Therapy should be capable of marked improvement by clinical application of experimentally proved treatment methods. That such improvement is necessary is apparent from study of mortality figures which range in the neighbourhood of 50% in most hospitals.[1, 17]

The value of such statistics is questionable, as many cases are lost in filing where a manifesta-

tion file is not kept, or incompletely kept.[22] A review of cases in the Victoria General Hospital, Halifax, for the period December 1, 1949, to August 31, 1951, revealed only 17 cases of acute pulmonary œdema, others certainly having been lost. Mortality was roughly 35%, with 6 deaths. The only case worthy of special mention was a 27 year old married woman, five months pregnant, admitted to the wards in severe dyspnœa with irritative cough, cyanosis and scattered rhonchi whose history and physical examination lacked any evidence of possible precipitating factor except that she had boiled soiled clothes in javel water in a small, unventilated kitchen. Despite conventional morphine and oxygen therapy, she progressed over a 48 hour period to full-blown acute pulmonary œdema which responded promptly, and within 24 hours permanently, to positive pressure oxygen therapy, in addition to the conventional measures. We used Barach's[18] mask as commercially available in this case, and also in a small group of post-myocardial infarction and hypertensive heart disease cases under emergency circumstances precluding adequate quantitative evaluation of the results.

We have been impressed by the rapid disappearance of frothing, the reduction and later disappearance of râles and the decrease in cyanosis, but would point out the risk of reducing the cardiac output excessively when this technique is combined with tourniquets on the extremities. Also the possibility of respiratory arrest from morphine depression of the respiratory centre combined with sudden removal of the stimulus of anoxia,[28] is to be remembered in prescribing the dose of opiate to be used with this method.

The pattern of peripheral vasoconstriction, under C.N.S. stimulation, with increased blood pressure and decreased ventricular output and increased pulmonary congestion produced in experimental animals,[19] fits the clinical picture as seen in most cases of acute pulmonary œdema. Spinal anæsthesia has been used clinically by Sarnoff and Farr[29] to lower the peripheral blood pressure and allow the Bainbridge reflex to reduce pulmonary congestion with satisfactory results in control of acute pulmonary œdema. Technical difficulties, however, limit the value of the procedure and this shortcoming applies even more markedly to sympathetic nerve blocks in the neck. More recently sympatholytic drugs, after successful animal use by many investigators,[24, 25, 26] have been given clinical trial, and Sarnoff[19] using RO-2-2222 has produced controlled degrees of systemic hypotension with clearing of acute pulmonary œdema, in hypertensive heart disease.

The results obtained in animals by Luisada,[17] using ethyl alcohol vapour inhalations as an anti-foaming agent, indicate clinical trial, as his survival rate increased significantly using alcohol alone, and was further increased by morphine; he feels that "the combination of all three remedies—morphine, oxygen under pressure, and alcohol vapours seems therefore to be indicated in clinical cases".

SUMMARY

It appears that two hundred years of increasing effort have failed to solve the problem of pathogenesis in acute pulmonary œdema. It has been learned, however, that the mechanism is certainly complex, probably a neurohemodynamic one in the majority of cases. Clinicians have failed to apply in large scale treatment investigation several experimentally valuable procedures, so that their life-saving potentialities remain essentially unexplored.

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CORTISONE IN ASTHMA*

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THE MAJORITY of reports in the literature during the past two years dealing with the subject of ACTH and cortisone in the treatment of bronchial asthma have been encouraging where ACTH has been used but less satisfying when cortisone has been used alone.

In 1950 Rose *et al.*[1] reported 6 cases of long-standing asthma treated with ACTH with good results; Carey *et al.*[2] reported a series of 19 cases of chronic intractable asthma of the intrinsic type treated with ACTH, all of whom improved, 15 obtaining complete remissions. 5 cases received cortisone alone and though all improved to a certain extent, only one had a complete remission; Randolph and Rollins[3] reported 5 cases of severe incapacitating asthma treated with intramuscular cortisone with only relatively effective results; Schwartz[4] (1951), on the other hand, obtained good results in 3 cases of chronic intractable asthma with oral cortisone, and Carryer *et al.*[5] (1950) reported 3 cases of the extrinsic type of asthma combined with hay fever due to ragweed sensitization, all of whom responded to cortisone given during the ragweed season. In 1951 Feinberg *et al.*[6] reported 15 cases of bronchial asthma treated with ACTH and cortisone, 6 of whom obtained complete relief (all on ACTH) and 4 obtaining incomplete relief—only one of whom was on cortisone alone; Cooke *et al.*[7] reported 31 cases of severe persistent asthma using ACTH or cortisone therapy and noticed substantial improvement in practically all cases.

Present series. — 21 patients with intrinsic bronchial asthma were studied who had been given courses of cortisone or combined cortisone and ACTH therapy. 18 of these cases were war veterans; 4 were females, 17 males.

The duration of asthma varied from a few months to 49 years; 4 cases had had attacks for a period of less than 2 years. The severity of the asthma varied from case to case, but the majority were of the severe intractable type with decreasing response to bronchodilators.

Ages of the patients varied from 18 to 69 years; 15 of these were over 40 years of age.

Two of the 21 cases reviewed had marked extrinsic factors. One (No. 3) had multiple positive skin tests to inhalants and several foods and attacks were usually precipitated by specific extrinsic factors. One (No. 5) had had seasonal ragweed asthma for many years before his asthma became perennial and continuous. Both of these patients responded well to therapy.

A total of 9 patients had positive skin tests, mostly to inhalants especially house dust.

12 patients had associated nasal conditions; 9 had deviated nasal septa, 5 had sinusitis and 3 had nasal polypi.

3 patients had allergic dermatitis.

There was a positive family history in 4 cases.

Treatment. — 17 of the patients were given cortisone by either the intramuscular or oral route. 2 (Nos. 2 and 4) were given ACTH for the first 2 days in conjunction with cortisone therapy; one (No. 16) was given ACTH after several days on cortisone while the cortisone dosage was gradually decreased, and one (No. 12) was given ACTH after an initial unsatisfactory trial of cortisone. Dosages of cortisone varied according to the response of the patient to the drug. Doses from 975 mgm. in 6 days to 3,250 mgm. in 33 days were given; and several patients were placed on maintenance doses for some considerable time from the commencement of treatment. Intramuscular cortisone was given in dosages of 200 mgm. for 2 days, then 100 mgm. daily, gradually reducing to 75 mgm. and 50 mgm. daily. Oral cortisone was given in dosages of 300 or 200 mgm. for the first day and thereafter reducing as above. It was found that in cases which responded, 200 mgm. as a commencing initial dosage was sufficient.

In the majority of patients, their weight, blood pressure, sputum and eosinophil percentage were measured daily. Several patients were too acutely ill for respiratory function tests to be instituted prior to therapy and therefore it has not been possible to correlate as a whole the response of the patient to cortisone with pre- and post-cortisone respiratory function studies. The studies undertaken were those of the vital capacity (usable) and maximum breathing capacity (grading percentage normal by Wright's formula), and in some, the percentage increase in maximum breathing capacity following the use of bronchodilators was assessed.

The response of the patient to the drug was assessed by (1) subjective relief and (2) objective relief, *i.e.*, diminished or absent râles in the lung fields; increase in chest expansion and reduction in amount of sputum.

Results.—Nine cases (Nos. 1 to 9 incl.) showed marked improvement, five cases (Nos. 10 to 14 incl.) showed very slight improvement and the seven remaining cases (Nos. 15 to 21 incl.) showed no improvement at all.

A. Those with marked improvement.—4 of the 9 cases obtained complete subjective and objective relief (Nos. 1 to 4 incl.). 2 of the 4 were

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Patient and age	Duration of asthma (years)	Etiology extrinsic and intrinsic	Other allergic manifestations	F.H.	Emphysema ++marked ++moderate ++early	Duration of chronic bronchitis (years)	Respiratory function % normal V.C.	Respiratory function % normal M.B.C.	Response to bronchodilators	Max. br. cap. % N after br. dilator	Drug	Dosage initial daily in mgm.	Total in mgm./days	Response subjectively and objectively	Respiratory function % N after cortisone V.C.	Respiratory function % N after cortisone M.B.C.	Mode of administration	Reactions	Eosinophils (% drop)	Duration of remission	Response to 2nd course
1 M. 18	14	I	Nil	Pos.	+	0	% N	% N	Good	56	Cortisone	200	1400/14	Complete S. and O.	% N 91	% N 43	Oral	None	44	Unknown	
2 M. 61	–1	I	Sinusitis and polypi	Neg.	+	4	73		Good initially Now poor		Cortisone and ACTH	200 and 100	1600/21 and 200 mgm.	Complete S. and O.	86	89	I.M.	None	75	3 weeks Post T.	Complete S. and O.
3 F. 23	21	E–I	Allergic dermatitis	Pos.	+	0			Good initially Now poor		Cortisone	200	1450/17	Complete S. and O.			Oral	None		3 months Post T.	
4 F. 33	6	I	Sinusitis and rhinitis	Neg.	+	0	85	81	Fair	86	Cortisone and ACTH	200 and 100	1600/17 and 200 mgm.	Complete S. and O.	89	112	I.M.	Irreg. menses Masculinity	43	3 weeks Post T.	Complete S. and O.
5 M. 69	49	E & I	Nil	Neg.	++	Few	59	16	Good initially Now poor	27	Cortisone	200	1750/16 +M	Complete S. Incomp. O.		34	I.M.	None	Rise	1 week Post T.	Temporary Complete S. and O.
6 F. 51	1	I	Allergic dermatitis	Neg.	++	8			Fair		Cortisone	200	1325/13	Complete S. Incomp. O.	52	37	Oral	None		2 months + Post T	
7 M. 27	8	I	Sinusitis and rhinitis	Neg.	++	0			Good initially Now poor		Cortisone	200	1625/15 +M	Incomp. S. and O.			Oral	None	34	Still on treatment	
8 F. 67	3	I	Allergic dermatitis. Sinusitis	Pos.	+	0			Good initially Now poor		Cortisone	200	975/6 +M	Incomp. S. and O.			Oral	None		3 weeks Post T.	
9 M. 56	9	I	Polypi	Pos.	++	6			Fair		Cortisone	200	1900/30	Incomp. S. only	51	71	I.M.	None	9	3 weeks Post T.	Incomplete S. only
10 M. 60	6	I	Nil	Neg.	++	37			Fair		Cortisone	200	2300/13 +M	Incomp. S. and O.			I.M.	None	Rise	1 month on T.	No relief
11 M. 51	32	I	Rhinitis and polypi	?Pos.	+++ 6 yrs.	6	59	16	Good initially Now poor	16	Cortisone	200	2350/20 +M	Incomp. S. and O.	70	32	I.M.	Slight œdema	59	3 months on T.	Diminishing
12 M. 46	5	I	Nil	Neg.	++	11	64	47	Good	53	Cortisone ACTH	200	3000/33 1.5 G	Incomp. S. and O.	54	35	I.M.	None	Rise	8 days on T.	
13 M. 50	9	I	Nil	Neg.	+++ 5 years	9	87	34	Good		Cortisone	300	1600/13	Slight S. only	122	48	Oral (Ex. 2 days)	None	Rise	0	
14 M. 53	–1	I	Nil	Neg.	++	11	60	37	Poor	30	Cortisone	200	2100/19	Slight S. only	55	39	I.M.	None	73	0	
15 M. 44	10	I	Nil	Neg.	+++ 10 years	10			Good		Cortisone	200	3250/33	No change	28		I.M. 18 Oral	Œdema hæmoptysis acne	Rise	0	
16 M. 45	3	I	Rhinitis	Neg.	++	10	75	31	Fair		Cortisone ACTH	300	3325/24 1 G	No change	73	32	Oral I.M.	None	62	0	
17 M. 59	59	I	Nil	Neg.	+++ 6 years	34	65	24	Fair		Cortisone	300	1600/13	No change	48	21	Oral (Ex. 2d)	None	3	0	
18 M. 54	3	I	Sinusitis	Neg.	+++ 3 years	11			Fair initially Now poor		Cortisone	200	1900/16	No change			I.M.	None	67	0	
19 M. 45	11	I	Nil	Neg.	++	11	42	44	Fair	48	Cortisone	300	1800/15	No change	59	46	Oral (Ex. 2d)	None	Rise	0	
20 M. 39	1–2	I	Nil	Neg.	+	7	99	70		88	Cortisone	200	1600/14	No change	100	66	I.M.	None	0	0	
21 M. 31	8	I	Nil	Neg.	+	0			Good initially Now poor		Cortisone	200	1400/13 + M	No change			Oral	None	53	0	

the only cases to receive ACTH for the first 2 days of therapy, in conjunction with cortisone. 2 patients (Nos. 5 and 6) had complete subjective improvement but the objective response was incomplete in that râles did never quite disappear on lung auscultation. 2 patients (Nos. 7 and 8) had considerable subjective and objective relief which was not complete, and one (No. 9) had considerable subjective relief only.

Relapses occurred in 6 of the 9 cases in varying intervals of 1 week to 3 months after therapy was discontinued. Four of these patients (Nos. 2, 4, 5 and 9) were given further courses; 3 of them obtained further complete subjective and objective relief and one (No. 9) again obtained further subjective relief. They are still on maintenance oral dosages of cortisone of 25 to 75 mgm. daily and improvement is maintained as long as the drug is given. No. 5 has been receiving cortisone for 10 months and continues to keep well.

Of the 3 patients who have not relapsed, No. 7 is still on treatment and No. 6 was given the drug too recently to assess the value. No. 1 discontinued treatment 6 months ago and has not reported for re-examination. It is felt that in his case the complete relief obtained may not have been due entirely to the cortisone as his symptoms became so severe even 2 days after cortisone was commenced that intravenous bronchodilators had to be given (cortisone was not stopped). He had also had a complete remission of symptoms for 9 months prior to his hospitalization, with a history of previous monthly attacks since the age of 4 years.

Three patients had allergic dermatitis; one since infancy, one intermittently for 5 years and one of 11 months' duration. In all 3 cases the skin condition improved slightly while treatment was being given.

Three of these 9 patients were given cortisone as an emergency measure because they were in a condition bordering on status asthmaticus: the first (No. 2) had had increasing disability with shortness of breath prior to admission and an acute asthmatic attack of 1 week's duration. He responded at first to bronchodilators but became refractory to them and 6 weeks later his condition became critical. He responded to cortisone and ACTH within 48 hours and obtained complete relief both subjectively and objectively within 9 days.

The second (No. 3) had had asthma since 2 years of age, averaging 1 attack/year usually precipitated by extrinsic factors. On this occasion she had a severe attack for 1 week prior to admission with a gradual worsening of her condition as she became refractory to bronchodilators. She obtained relief within 24 hours on cortisone alone, and had no further attacks until 3 months after therapy had been discontinued.

The third (No. 9) had had asthma for 9 years with attacks increasing in severity and frequency. He showed considerable improvement on cortisone, but relapsed to his former state 3 weeks after therapy had been discontinued. The attacks then increased and became so severe that when he was admitted to hospital 2 months later he was averaging 6 or 7 attacks daily. On this occasion he was given oral cortisone and again obtained marked subjective relief.

B. Those with very slight improvement.—Of the 5 patients who showed very slight improvement with cortisone, 2 obtained considerable subjective and objective relief within 4 days, which lasted for 34 days in patient No. 10 and 3 months in patient No. 11 (but No. 11 is very suggestible). At the end of those periods, while still on treatment, both had respiratory infections, and when given further courses of cortisone after the infections had subsided, no material benefit was obtained. One patient (No. 12) also obtained considerable subjective and objective relief which lasted for 8 days, after which he became feverish and more dyspnœic and cortisone was discontinued. ACTH was then given a trial with some slight subjective improvement only, and he relapsed back to his former state 2 weeks after therapy was discontinued. Two patients (Nos. 13 and 14) obtained slight subjective relief from cortisone, but insufficient to warrant continuation of the drug.

C. Those with no improvement.—7 of the 21 cases had no beneficial response to cortisone.

Emphysema.—The majority of patients who had only slight or no improvement with cortisone suffered from severe emphysema and a long history of chronic bronchitis prior to the onset of asthmatic symptoms. The severity of the emphysema was assessed clinically, radiologically and by respiratory function tests with the following results:

Five had marked emphysema of long duration. These showed slight or no improvement.

Five had a moderately severe degree of emphysema and a history of chronic bronchitis

of over 10 years' duration. These showed slight or no improvement.

Four had a moderately severe degree of emphysema but with a history of chronic bronchitis of under 10 years' duration. These showed considerable improvement, but incomplete in all.

Seven had early or slight evidence of emphysema. 5 of these showed marked improvement, 4 of whom were the only cases reported who obtained complete subjective and objective relief. One of the cases who did not respond had had a left lower lobectomy for bronchiectasis 3 years before. (No. 20).

These findings confirm those in a previous report by Feinberg *et al.*[6] who stated that 2 of their failures occurred in patients with long histories and evidence of severe emphysema.

Conditions other than asthma which were present in those cases which did not respond to the drug were: (1) Hypertensive cardiovascular disease (1 case) No. 11. (2) Previous lobectomy for bronchiectasis (2 cases) Nos. 10 and 20. (3) Psychogenic element (2 cases) Nos. 11 and 12.

Eosinophil count.—It will be noted from the chart that we have not found the percentage drop in eosinophils during treatment to be a necessary indication of a good response to the drug. This confirms previous reports (Feinberg *et al.*;[7] Cooke *et al.*[7]).

Day of maximum improvement.—All cases who showed some improvement under therapy, either poor and temporary or complete, responded markedly within 24 hr. to 6 days and their maximum benefit was attained within 3 to 9 days after therapy commenced, except in No. 4 in whom complete subjective and objective relief was not obtained till the 17th day, and in No. 7 who did not reach his maximum till the 12th day.

Side effects were only observed in 2 cases; one of whom (No. 4) is a woman aged 33 years and has been on maintenance dosage of cortisone for 5 months. She has suffered from menstrual irregularities throughout, and 4 months after treatment commenced, noticed increase in facial and chest hair. The other patient (No. 15) had marked œdema and hæmoptysis and the drug was discontinued. He also developed acne. Of the other 3 cases who have been on maintenance dosages for 4 to 10 months' duration, no side effects have as yet been observed.

CONCLUSIONS

1. It would appear that cortisone has a definite rôle to play in the treatment of cases of intrinsic bronchial asthma whose emphysema is not severe enough to cause irreversible changes in their lung fields.

2. It may be a life-saving measure in those patients in status asthmaticus who do not respond to bronchodilators; and as in the 3 cases described, the response to cortisone can then be dramatic.

3. The response to the drug is more or less unpredictable. Many more cases should be studied before its full value in asthma can be assessed.

4. Cortisone was found to be just as effective given orally as by the intramuscular route. Dosages of 200 mgm. for 1 day, decreasing to 100 mgm. daily for several days thereafter were sufficient.

5. The majority of cases relapsed in 1 week to 3 months after cortisone had been discontinued. As it would appear that maintenance doses have to be continued in all cases which respond to the drug, cortisone should only be tried in those patients in whom all other forms of medication have failed.

6. Side effects were not frequent. One patient has been taking cortisone for 10 months without ill effect.

This study was assisted by a Grant in Aid from the Hutchison Fund, McGill University.

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ERRATUM

Studies on the Excretion of Cortisone and Compound F using the Porter-Silber Method by K. K. Carroll, H. T. McAlpine, and R. L. Noble (*Canad. M. A. J.*, 65: 363, 1951).

In Figure 1 the scale for concentration in urine should read 0.05, 0.1, 0.15, 0.2, 0.25 mgm./100 ml. of urine instead of 0.1, 0.2, 0.3, 0.4, 0.5 mgm./100 ml. as reported. Since the incorrect scale was used in the calculation of the results reported for human urines, the correct values are one-half the reported values.

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EARLY AMBULATION FOLLOWING ABORTION*

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THIS PAPER comprises a study of 200 cases of incomplete and complete abortion in an attempt to justify two premises on which the treatment of such cases is based when admitted to the public ward of the Victoria General Hospital, Halifax. The two premises are: (1) Early ambulation and early discharge from hospital; (2) exploration of the uterus under anæsthesia only when it is felt that definite products of conception remain, or for persistent bleeding, but not as a matter of routine in all cases.

Material.—The case histories of 280 married public ward patients were reviewed and a questionnaire sent to each patient. From this number we obtained 200 follow-ups, the remainder we were unable to trace because of change in address. Septic cases were eliminated as the treatment of these differs from the non-septic in our hospital. We realize it is difficult, in many instances impossible, to distinguish between an infected and a non-infected abortion. A combination, however, of (a) a temperature of 100 degrees or more, (b) a foul discharge vaginally, and (c) tenderness on moving the cervix or when palpating the parametrial areas during vaginal examination places the case in an infected category so far as we are concerned. We have made little use of cervical or uterine cultures as a method of distinguishing between the septic and the non-septic abortion.

We also eliminated the single woman from this study, feeling that any attempt to follow up these cases might prove embarrassing to the individual. Our follow-up questionnaire was prepared with a view to obtaining the following information; a great many of the women were contacted directly as well:

1. When the bloody discharge had cleared up completely.

2. Whether the patient had returned to one of the other hospitals for treatment, or had to be treated by her family physician.

3. When she felt like resuming all of her usual daily activities.

4. Whether she had become pregnant again; and, if not, was this due to some form of birth control.

5. Finally, whether the patient liked the program of early rising and early discharge from hospital.

Treatment.—On admission to hospital each case of incomplete or complete abortion is treated as follows:

(a) Complete physical examination by the intern including blood picture, Kahn, and urinalysis, with cross-matching of blood for transfusion if the Hgb. is below 70%, or if the patient is bleeding excessively.

(b) Examination in the treatment room without anæsthetic and removal of any loose tissue in the vagina or cervix with sterile ovum forceps. We feel that many of these women bleed because tissue is caught up in the cervical canal preventing the uterus from contracting down. We believe the removal of such tissue with ovum forceps is a simple matter, and once it is removed, the bleeding usually stops and to all intents and purposes the case is complete.

(c) Following examination in the treatment room, if it is still felt that the case is incomplete because of some combination of the four factors of (1) bleeding, (2) big uterus, (3) cramps, and (4) failure of the cervix to close, the remaining tissue is removed under anæsthesia with ovum forceps. Occasionally curettement is performed.

(d) Those cases completed in the treatment room without anæsthesia are allowed up, and in many instances discharged from the hospital the same day. Those completed under anæsthesia are discharged the following morning. The patients are allowed up immediately or after recovering from anæsthesia and have complete ambulatory freedom, including bathroom privileges.

(e) Blood transfusions are used liberally. Any patient with a Hgb. of less than 70% receives sufficient blood to bring the Hgb. up to this level.

RESULTS

Table I shows that of the 200 cases reviewed, 41, or 20.5%, were complete upon arrival in the hospital or completed themselves shortly after admission. Sixty-nine, or 34.5%, were completed in the treatment room by removal of tissue from the cervical canal with ovum forceps and without anæsthetic. Ninety, or 45%, underwent operative removal under anæsthesia, 10 of which proved negative for products of conception.

*Presented before the annual meeting of the Canadian Society of Obstetricians and Gynæcologists at the Seigniory Club, Quebec, June, 1951.

Ten of the 200 patients under consideration had to return to hospital because of bleeding. Three of these had undergone operative removal of the placenta (or part of it) under anæsthetic at their first admission. In two of these three cases placental tissue was obtained at the second try. Of the remaining seven patients who had to be re-admitted—patients we had felt were complete, or completed in the treatment room without anæsthesia—five showed placental tissue when emptied under anæsthesia.

TABLE I.

TREATMENT OF CASES

	Number	*Percentage of total*
Complete on arrival at hospital	10	5.0
Completed themselves in hospital	31	15.5
Completed in treatment room	69	34.5
Operative removal under anæsthesia	90	45.0
Total	200	100.0

Table II shows that in 189, or 94.5%, of the patients the bloody discharge had disappeared completely within four weeks, and in only 11, or 5.5%, did it persist longer.

TABLE II.

BLOODY DISCHARGE

	Number	*Percentage of total*
Cleared up completely within 4 weeks	189	94.5
Cleared up completely within 5 weeks	2	1.0
Cleared up completely within 6 weeks	7	3.5
Cleared up completely within 8 weeks	2	1.0
Total	200	100.0

Table III reveals that 171, or 85.5%, of the patients were able to do all of their own work in 4 weeks or less, while only 29, or 14.5%, required more than 4 weeks before they felt strong enough to perform all of their usual daily activities.

Sixteen, or 8%, returned to their family doctor for reasons directly connected with the abortion. Of these 16 patients, 2 were treated for a mild pelvic infection, 7 were treated for the bloody discharge, and only 7 had to return to hospital for bleeding. It was stated above that 10 patients returned to hospital but 3 of these did so directly without seeing their own doctor (Table IV).

Regarding future pregnancies, (Table V) 124 of these abortions occurred in 1949-1950 and 76 in 1947-1948, so we feel that sufficient time has not yet elapsed to see if our form of treatment has had any detrimental effects on the fertility

TABLE III.

RETURN TO WORK

	Number	*Percentage of total*
Performed all duties within 1 week	86	43.0
Performed all duties within 2 weeks	31	15.5
Performed all duties within 3 weeks	16	8.0
Performed all duties within 4 weeks	38	19.0
Performed all duties within 4 plus weeks	29	14.5
Total	200	100.0

TABLE IV.

COMPLICATIONS

	Number	*Percentage of total*
Returned to hospital because of bleeding	10	5.0
Treated for pelvic infection	2	1.0
Treated for bloody discharge—medically	7	3.5
	19	9.5

TABLE V.

FERTILITY

	Number		*Percentage of total*	
Pregnant again since abortion		84		42.0
Full term delivery	55		65.4	
Pregnant at time of writing	12		14.5	
Aborted again	17		20.1	
Total	84		100.0	
Not pregnant since abortion		116		58.0
Using birth control	55		47.4	
Not using birth control	61		52.6	
	116		100.0	100.0

of these women. 84, or 42%, of the patients have been pregnant since their abortion, and of these 55, or 65.4% have delivered full term babies; 17, or 20.1%, aborted again; and 12, or 14.5% are

pregnant at the time of the writing of this paper. Fifty-five, or 47.4%, of the 116 patients not yet pregnant are using some form of birth control.

TABLE VI.

EARLY AMBULATION AND EARLY DISCHARGE

	Number	*Percentage of total*
In favour of early ambulation and early discharge	144	74.0
Not in favour of early ambulation and early discharge	56	26.0
Total	200	100.0

One hundred forty-four, or 74%, of the patients were definitely in favour of the early rising and early discharge from hospital, whereas 55, or 26%, were against the program (Table VI). The reasons the latter group gave were varied but mainly centred around "weakness". In general this did not appear to be related to blood loss since only 12 of this group, or 21.4%, required blood transfusion.

COMMENT

The Department of Obstetrics and Gynæcology of Dalhousie University has been interested in early ambulation in the puerperal woman for over twenty years, and recently did a survey and a follow-up of about 1,200 public ward women covering the period 1928-1945, to determine if this procedure causes an increase in immediate or late morbidity or disability. The experience with early ambulation in the full term puerpera suggested that the same program might be well worthwhile following a miscarriage. The above survey showed that early ambulation did not increase the tendency to morbidity, and the impression gained was that it actually decreased it.

The great advantage of early ambulation is an economic one. In these days of high hospital costs and the difficulty of obtaining domestic help, it is a great advantage to a young woman in the child bearing age to be able to remain in hospital only a day or two and then to be more or less capable of looking after herself and her family from the day she goes home. All this represents a real saving of money and removes a good deal of the usual expense and inconvenience of having a miscarriage. We also feel this short hospital stay and early return to normal living minimizes the psychological traumata due to the accident, which in some cases is probably more than we generally think. This, also, is a decided gain.

The greatest risk in this program is probably that of hæmorrhage. Each woman on leaving the hospital is instructed to return immediately or to consult her own doctor if there are any signs of hæmorrhage or if bleeding persists for more than two weeks. As noted above, we had to readmit only 10 patients for persistent bleeding, 7 of which were due to retained fragments of placenta. We do not believe early ambulation increases the tendency to infection: on the contrary we believe the improved drainage due to the upright position and the more active contractions of the uterus decrease such a tendency. In our 200 cases there were only two cases with mild pelvic infection, an incidence of 1%.

It is our impression and their own statement that most women prefer this type of regimen, and that they feel better at the end of a week than after the traditional period of rest in bed.

We know that some women will leave hospital under this policy with a fragment of placenta still attached. We do not believe, as many textbooks state, that retained placenta causes infection *per se*, but only when it blocks the cervix and dams back secretion, and then usually only causes a mild sapremia. In the latter case, that is where a piece of placenta blocks the internal os, it can be felt through the cervix on predischarge examination and removed with ovum forceps. A piece of placenta retained high up in the uterus which cannot be felt through the cervix and from which drainage is free, does not in our experience cause infection, and in the vast majority of cases will be passed with few untoward effects. If it is not passed, bleeding will continue and require operative removal.

We take no definite stand on the operative versus the wait-and-see or conservative method of treating incomplete abortions. Table VII shows that in the first 84 cases coming under this survey the prevailing regimen was wait-and-see, while in the remaining 116 cases we emptied more uteri by operation, largely because there was a more urgent call on our available hospital beds. We do not feel there are sufficient cases to make the figures of Table VII significant statistically. However, if we were asked to take a stand, we would probably favour the wait-and-see policy—the administration of oxytocics in an attempt to influence the uterus to empty itself

without instrumental aid. We would interfere only to remove with ovum forceps and without anæsthesia placental fragments that could be felt through the dilated cervix, leaving any other fragment to look after itself, except in the case where it causes continued bleeding. We are still not sure that dilatation and instrumental removal of placental tissue, particularly when accompanied by curettage, does not interfere with future fertility.

TABLE VII.

CONSERVATIVE VERSUS OPERATIVE REGIMEN

	1947–1948		*1949–1950*	
	Cases	*%*	*Cases*	*%*
Number of cases treated	84	100.0	116	100.0
Operative treatment under anæsthesia	28	33.3	62	53.4
Re-admitted	1	1.2	9	7.8
Pelvic infection	1	1.2	1	0.9
Treated for bloody discharge—medically	1	1.2	6	5.2

All products removed in the treatment room, or in the operating room under anæsthesia, were examined by the Department of Pathology. There were no cases of chorionepithelioma.

My sincere thanks to Drs. H. B. Atlee and K. M. Grant of the Department of Gynæcology of the Victoria Hospital, Halifax, for their help and criticism in the preparation of this paper.

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FURTHER STUDY OF BLOOD CHOLESTEROL IN SCHIZOPHRENIA*

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IN A PREVIOUS WORK,[1] the authors have observed an increased *variability* of blood cholesterol levels in a group of schizophrenics, as compared with normal subjects. The mean variation percentages in a group of ten subjects were 7.54 and 13.66% for total cholesterol and cholesterol esters respectively, while a normal group (8 subjects) showed variations of only 6.02 and 7.49% for the same constituents. At that time, other investigators had already drawn the attention to this greater variability of metabolic constituents in mentally deficient individuals.[2]

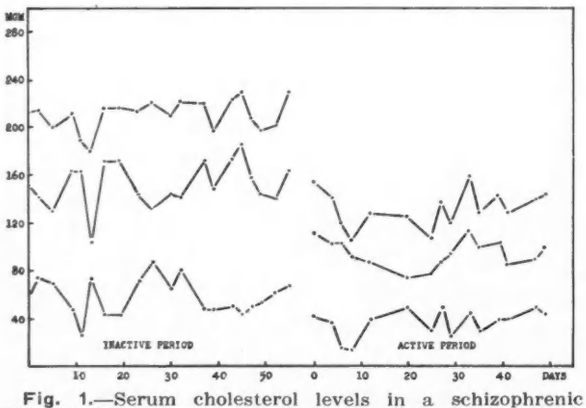

Fig. 1.—Serum cholesterol levels in a schizophrenic (Obs. 1) during inactive and active periods. In this graph and the following, the top curve represents total cholesterol level; the middle curve, cholesterol esters level; and the bottom curve, free cholesterol level.

In nine out of the ten chosen subjects, there was also observed a definite parallelism between the total cholesterol and the cholesterol esters levels (Figs. 1 and 2), an indication that the esters level is the most readily altered. Calculation of the correlation coefficients to illustrate this parallelism revealed another peculiar behaviour of the schizophrenic group. It was found that this coefficient was nearly identical for every individual in the group, regardless of their respective cholesterol levels (Table IV). Such a similarity was not observed in the normal group. We then suggested that we had been dealing with a rather homogeneous biological, if not mental, group.

Two hypotheses arose immediately. Could

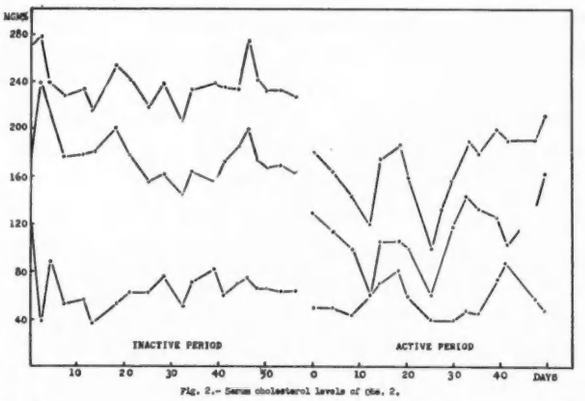

Fig. 2.- Serum cholesterol levels of Obs. 2.

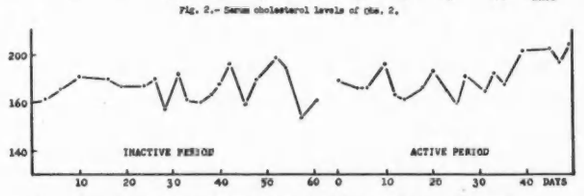

Fig. 3.—Serum total cholesterol level in Obs. 10.

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this similarity be attributed (1) to a lack of metabolic adaptability concomitant with mental deficiency, or (2) merely to the fact that all the individuals in this particular group were being subjected for quite a number of years to the same standards of living, such as diet, environment, relative physical inactivity, etc.? The most evident way to verify this last hypothesis was, as then suggested, to undertake a new investigation on the same group submitted this time to a mild physical activity. This procedure however, if likely the most conclusive, would not be an easy one. We were dealing with chronic patients, most of them catatonic and physically inactive for a number of years. Accordingly no fixed program could be scheduled.

We were fortunate enough to perform this experiment at exactly the same time of the year (from January to March) as in the previous study and with the same group. This, we thought, would surely eliminate variations due to such cumbersome factors as weather, seasonal diet, etc.

Before starting the experiment itself, we submitted the group to various trials. At first the patients were not compelled to strenuous exercises. They began with a simple walk of about one-half hour. During the first two days, the subjects seemed rapidly exhausted and retired each night much earlier than usual. A few even showed a slight increase in body temperature. About ten days were spent in having the group perform a serious training. Surprisingly. snow shovelling proved to be the most efficient subterfuge to gain the co-operation of the patients. They were then more easily controlled and, on the whole, would be quite active for about two hours a day, one hour in the morning and one hour in the afternoon. This schedule was followed 6 days each week.

TABLE I.

Obs.	*Age*	*Body weight (lbs.)*				*Behaviour*	
		1st day	*15th day*	*25th day*	*Last day*	*Before experiment*	*At end of experiment*
1	36	154	153	155	152	Hebephrenia. Impulsiveness.	No improvement.
2	45	150	149	146	150	Inactivity. Total indifference.	Slightly active.
3	40	132	131	135	135	Hebephrenia. Mutism. Inactivity.	Tremendous appetite.
4	25	136	134	138	140	Hebephrenia and catatonia. Soliloquy. Complete indifference.	Better contact with environment. Less frequent soliloquy.
5	20	113	111	115	123	Hebephrenia and catatonia. Agitation. Anorexia.	No improvement, except better appetite.
6	26	133	132	136	135	Feeblemindedness. Apathy. Indifference.	Increased activity. Better appetite.
7	24	109	108	107	117	Catatonia. Complete mutism. Anorexia.	Mutism. More active. Good appetite.
8	27	130	129	130	130	Hebephrenia. Complete inactivity. Gatism.	No improvement.
9	28	126	121	123	124	Hebephrenia and catatonia. Negativism.	More active.
10	28	117	114	118	117	Hebephrenia and catatonia. Gatism. Impulsiveness.	Improved appetite. More active.

During the first two weeks, as shown in Table I, the body weight dropped slightly (from 2 to 6 pounds). There was a transitory, but still noticeable improvement of the mental state. Table I gives the main clinical data before and during the experiment. In five patients the body weight had increased at the end of the experiment (from 2 to 10 pounds) and had remained stationary in three others. The appetite was significantly improved, especially in one patient (Obs. 3). For the first time in years, all the patients managed quite well to eat by themselves. The experiment continued for ten weeks.

The first samples of blood were collected on

the 18th day of the experiment (this step was not begun earlier, in anticipation of the great number of specimens to be collected) and cholesterol determinations were made about every other day for the next eight weeks. Here are our main observations:

1. As was expected, there were spectacular drops in the cholesterol levels (as much as 36.4% for total cholesterol and from 9.6 to 39.3% for cholesterol esters). Figs. 1 and 2 clearly illustrate these drops. In one of the patients (Obs. 4), the total cholesterol dropped as low as 79 mgm. per 100 ml. of serum three weeks after the onset of the experiment. Yet a thorough physical examination revealed no cause of alarm. Three weeks later however the cholesterol had reached its primitive level. Only one patient (Obs. 10) behaved quite differently. This case is developed below.

2. In spite of an increased ingestion of food and an increased body weight in most subjects, the cholesterol levels were still low after 8 weeks, except in one case (Obs. 10). In the remaining nine subjects, six reached subnormal cholesterol levels (less than 150 mgm.) without apparent physical discomfort. Only one patient (Obs. 4) had had a subnormal cholesterol level before the experiment.

3. The previously observed *variability* of cholesterol levels was greatly emphasized during the period of physical activity (Tables II and III). It is interesting to compare such variation percentages as high as 20.65% for total cholesterol and 35.50% for cholesterol esters, with those of the normal individuals all of whom, it is to be remembered, were then submitted to a constant physical activity. The mean variation percentage of total cholesterol which had been 7.54% before the experiment as compared with 6.02% for the normal group, rose to 11.51%. Meanwhile the variation percentage of cholesterol esters jumped from 13.66 to 18.31%. The mean variation percentage for the normal group had been 7.49% for the same constituents.

4. As we had already observed, marked peaks appeared now and then in the cholesterol curves (Figs. 1 and 2). These had never been observed in the normal ones.

5. No indication could be found in the results as to which fraction of the cholesterol was preferably removed from the blood under this stress. Percentages of drops from the primitive levels are highly variable (Tables II and III).

6. The parallelism between the total cholesterol and the cholesterol is still apparent, as indicated by a relatively high correlation co-

TABLE II.

	Before experiment			*During experiment*			
Obs.	*Mean total cholesterol*	*Standard error*	*Variation percentage*	*Mean total cholesterol*	*Standard error*	*Variation percentage*	*Percentage of drop*
1	211.0	3.079	**6.53**	135.0	4.160	**11.13**	36.0
2	238.0	4.235	**7.95**	179.0	3.507	**12.06**	24.8
3	204.5	3.992	**8.51**	155.5	3.974	**8.08**	23.9
4	119.0	2.610	**8.18**	102.0	5.437	**20.65**	14.3
5	163.0	2.825	**7.15**	126.5	4.480	**11.23**	22.4
6	164.0	2.980	**8.13**	120.0	3.758	**11.27**	36.4
7	175.0	3.162	**7.45**	165.0	4.605	**9.67**	5.6
8	154.0	2.977	**7.49**	112.0	4.054	**12.53**	27.3
9	161.0	2.189	**6.23**	135.0	4.022	**10.74**	16.2
10	172.0	2.989	**7.77**	190.5	3.210	**7.72**	−10.7
		Mean:	**7.54**		Mean:	**11.51**	

TABLE III.

	Before experiment			*During experiment*			
Obs.	*Mean chol. esters*	*Standard error*	*Variation percentage*	*Mean chol. esters*	*Standard error*	*Variation percentage*	*Percentage of drop*
1	152.5	4.446	**13.04**	92.5	3.182	**12.40**	39.3
2	173.5	4.970	**12.81**	124.0	4.124	**16.38**	28.6
3	149.0	4.281	**12.52**	112.0	4.272	**17.70**	24.8
4	73.0	3.678	**18.84**	66.0	4.049	**35.50**	9.6
5	116.5	4.157	**14.71**	81.0	3.130	**31.80**	30.4
6	112.0	3.763	**15.03**	85.0	3.825	**16.22**	33.0
7	120.0	4.300	**14.77**	125.0	2.607	**7.22**	−4.2
8	100.0	3.537	**13.70**	72.5	3.680	**17.61**	27.5
9	109.0	2.479	**10.42**	98.5	4.482	**16.41**	9.6
10	124.0	2.985	**10.77**	139.0	5.870	**11.91**	−12.1
		Mean:	**13.66**		Mean:	**18.31**	

efficient (Table IV). This parallelism is graphically expressed in Fig. 1. But the similarity of coefficients is no longer existent. Due to the limited time of the experiment, it is difficult to compare these with the normal ones. Nevertheless if this coefficient appears to be highly variable with individuals under physical activity, it seems, according to our limited data, constantly higher in the schizophrenics.

TABLE IV.

CORRELATION COEFFICIENTS OF TOTAL CHOLESTEROL AND CHOLESTEROL ESTERS

Schizophrenic group			*Normal group*	
Obs.	*Inactive period*	*Active period*	*Obs.*	
1	0.60	0.69	1	0.25
2	0.60	0.73	2	−0.23
3	0.595	0.45	3	0.36
4	0.66	0.81	4	−0.43
5	0.64	0.42	5	0.44
6	0.66	0.66	6	0.08
7	0.66	0.42	7	0.27
8	0.60	0.51	8	0.20
9	0.345	0.69		
10	0.67	0.57		

7. *Observation 10.*—Strangely enough, one patient showed a definite *increase* in his cholesterol levels during the experiment (Fig. 3). The mean total cholesterol jumped from 172.0 to 190.5 mgm. (Table II) and the cholesterol esters from 124.0 to 139.0 mgm. (Table III). In addition to this peculiarity, this patient was the only one to show a practically identical correlation coefficient during both active and inactive periods (Table IV), as well as nearly constant variation percentages both in total cholesterol and cholesterol esters (Tables II and III). This subject, 28 years old, has been diagnosed as an hebephrenocatatonic schizophrenic for the last ten years. During the experiment he did not behave differently from the others. He was rather active and ate well. But there was at no time an indication of discrepancy from the rest of the group.

8. *Observation 6.* — This subject whose behaviour suggested schizophrenia, had been diagnosed previously as feebleminded. The absence of discrepancy in the data obtained in this case seems to suggest that such a peculiar behaviour of the metabolic constituents is not restricted solely to schizophrenics but to some other mental deficiencies as well.

Two months after the end of the experiment, a thorough mental examination of the group showed no improvement whatsoever, but a complete regression to the previous state.

SUMMARY AND CONCLUSIONS

Owing to the particular type of patients we have been dealing with, the experiment unfortunately had to be limited in time. Otherwise we might have been fortunate enough to collect interesting data on their metabolic adaptability. Nevertheless a few physiological observations can be recorded.

1. The greater variability of metabolic constituents in mental deficiency as observed previously is reaffirmed under totally different conditions. However this behaviour does not seem limited to schizophrenia. Favouring this last hypothesis is Obs. 6.

2. Dealing with subjects submitted to a temporary physical effort after years of inactivity, is quite exceptional. The rapid and spectacular drops of cholesterol levels should be interesting to physiologists.

3. In spite of an increased ingestion of food, these levels remain abnormally low even after 8 weeks. During the same period, the body weight showed, on the contrary, a slight tendency to increase.

4. The similarity of correlation coefficients between total cholesterol and cholesterol esters previously observed is no longer existent. Nevertheless a definite parallelism between the same constituents is still evident, an indication that the ester fraction is chiefly responsible for the variability of total cholesterol.

5. The discordance of correlation coefficients under physical activity should emphasize the danger of drawing too hasty conclusions. Other factors than the mental condition might be responsible for the similarity of compiled data, especially with ward patients. Such an investigation is still being pursued.

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It is the privilege of every human work which is well done, to invest the doer with a certain haughtiness.—Emerson.

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SYPHILITIC CARDIOVASCULAR DISEASE

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CARDIOVASCULAR DISEASE in the syphilitic patient frequently gives rise to difficulties in assessing the degree to which syphilis is the responsible cause, and in estimating the prognosis and the type of treatment that should be given.

For this reason, it was decided to collect as detailed information as possible from a consecutive group of cases examined and diagnosed at the Vancouver Venereal Disease Clinic over a period of eight years (1942-49), and to draw what conclusions were possible from this material. It was unfortunately necessary to omit possibly an equal number of cases from this study either on account of an almost complete absence of recorded information, or because the patients were treated as "possible" or "suspected" aortitis on a precautionary basis, without any sound corroborative evidence.

It should be stressed, however, that the syphilitic patient may have cardiovascular disease of other etiology which bears no relation to the syphilitic infection. Alternatively, such non-syphilitic disease may coexist with, and modify the clinical findings and progress of syphilitic cardiovascular disease. For this reason, anti-syphilitic treatment in a case of advanced cardiovascular syphilis must be considered of very secondary importance compared with the treatment of the patient on general medical or cardiac lines.

In the present study, 108 consecutive cases of syphilitic cardiovascular disease were reviewed. The ratio of male to female was approximately 6 to 1 (93 male, 15 female). Apart from one man aged 28, who suffered with a congenital infection, the ages on first coming under observation ranged from 40 to 70 and over, with the average age of this series being 57 years.

There was no significant difference between the average ages of males and females in the series. The patients were divided into five groups according to the stage and type of syphilitic involvement, and it was found that this average age was the same for all groups.

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TYPES OF LESION

The groups into which these cases were divided are as follows:

	Cases
Simple aortitis	22
Mild aortic dilatation (uncomplicated)	11
Aneurysm (alone)	22
Aneurysm plus aortic regurgitation	28
Aortic regurgitation (without aneurysm)	25
Total	108

The diagnosis of simple aortitis has for long been a subject for controversy, with the interpretation of findings dependent upon the experience and enthusiasm of the observer. In this series of cases, however, the diagnosis has been based upon: (1) A positive blood serology or a history of inadequately treated syphilis. (2) Some dilatation, with increased pulsation of the aorta on fluoroscopic examination. (3) The presence of an accentuated aortic diastolic sound (particularly in the absence of hypertension) or an aortic systolic murmur. (4) Possibly symptoms of chest pain.

No cases were admitted for this study unless they showed definite evidence of the first three of these essential criteria.

Simple dilatation, for the purposes of this study, is a term which has been applied to those cases of advanced aortitis, in which dilatation has become more marked but is not considered sufficient to describe as an aneurysm. The distinction between simple dilatation and aortitis or aneurysm is therefore an arbitrary one, and borderline cases must obviously occur in which the classification has been difficult to make and the choice has necessarily been a personal one.

In view of these definitions, it may be pointed out that *all* cases of syphilitic aortic disease, at the stage when it can be definitely recognized as such by the physician of average skill, show some degree of aortic dilatation (with increased pulsation in the early stages) on fluoroscopic examination. This is perhaps one of the outstanding features which may help to distinguish syphilitic from other types of cardiovascular disease.

Reference to the numbers of cases in each category will show that in this series 53 cases (49%) had aortic regurgitation, and that 28 of these patients were also suffering with gross dilatation or aneurysm of the aorta.

DURATION OF INFECTION BEFORE DISCOVERY OF THE AORTIC LESION

In only 47 cases (44%) was there any record of the duration of infection, and in a few of these instances the duration recorded was an estimated minimum.

Those reporting with aneurysm alone or with a combination of aneurysm and aortic regurgitation were of longer average duration than those showing aortitis with simple dilatation or aortic regurgitation alone.

Duration of infection. — Aneurysm (with or without aortic regurgitation), 31 years (av.). Simple aortitis, dilatation, or aortic regurgitation, 22 years (av.).

It appears to have been unusual in this series to detect any definite aortic change in less than 10 years after the original infection.

It remains to be seen whether adequate treatment with penicillin will materially alter the incidence of cardiovascular disease due to syphilitic infection, or whether it will be shown to arrest the progress of the damage in those with early established aortic changes.

Blood serology. — Two serological tests were done on every patient—a Kahn and complement fixation. The findings are shown in the following table:

TABLE I.

Kahn test		
was positive in	102 cases	94%
and doubtful in	3 "	3%
Complement fixation		
was positive in	88 "	82%
and doubtful in	10 "	9%
Both tests were negative in	3 "	3%

In this series only 3 cases (3%) were negative to both tests.

Kahn tests were positive or doubtful in 97% of cases; whereas the complement fixation test was apparently a little less sensitive, being positive or doubtful in 91%. Two of the 3 cases which were negative to both tests were suffering from manifestations of neurosyphilis in addition to their cardiovascular changes. Both had, at the time of their diagnosis, received a negligible amount of treatment with bismuth alone.

Symptoms. — Enquiries were made in every case regarding complaints of shortness of breath on exertion, palpitations, chest pains or angina, œdema, etc. Reference to Table II will show, as was to be expected, that those with little or early structural damage did not complain of marked symptoms; whereas, a very much higher percentage of those with later and more severe damage admitted complaints at their first attendance.

Pain.—Although pain has been occasionally mentioned as a frequently-occurring symptom in early syphilitic disease of the aorta, this has not been confirmed in the present series of cases.

TABLE II.

	Symptoms		*No symptoms*	
	Number	*Percentage*	*Number*	*Percentage*
Simple aortitis	7	32	15 (0)	68
Simple dilatation	4	36	7 (0)	64
Aortic regurgitation	21	84	4 (1)	16
Aortic regurgitation plus aneurysm	21	75	7 (4)	25
Aneurysm alone	19	86	3 (0)	14

(Figures in parenthesis represent the number of patients among those originally not complaining of symptoms who have since died *of their cardiovascular disease.*)

Chest pain was noticeably absent in patients suffering with the earlier manifestations of syphilitic aortic disease, while those in whom pain was a feature were found in a fair proportion of instances to be suffering with other conditions such as severe hypertensive heart disease or coronary artery disease, which were probably responsible in some degree, if not entirely, for their pain.

The presence of hypertension and of atherosclerosis of the coronary arteries as independent conditions in patients suffering with syphilitic disease should not be overlooked, and should always be considered as a possible additional cause of pain.

TABLE III.

CASES OF SYPHILITIC CARDIOVASCULAR DISEASE IN WHICH CHEST PAIN WAS A FEATURE

Type of lesion	*Total No. of cases*	*Pain*	*Additional information*
Simple aortitis	22	2	1 had myocardial infarction.
Simple dilatation	11	3	2 had severe hypertension.
Aortic regurgitation	25	9	All 9 had atherosclerosis, hypertension or myocardial infarction.
Aneurysm	22	10	1 hypertension. 1 hypertension plus anterior infarction.
Aneurysm plus aortic regurgitation	28	9	2 hypertensives (severe) died of congestive heart failure.

The pain resulting from purely syphilitic changes most frequently occurred late in the disease, when structural damage was considerable, when marked pressure symptoms developed due to aneurysms, or when myocardial embarrassment became pronounced.

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Calcification.—It is difficult to decide the underlying factors responsible for the development of calcification in syphilitic disease of the aorta, and an analysis of these cases does not appear to throw much light on the subject. Reference to Table IV will indicate that those cases with the more advanced stages of cardiovascular syphilis appear to have had a higher percentage of calcification than those with little structural damage. This is perhaps only to be expected.

TABLE IV.

	No. of cases	*Calcification*	*Percentage*	*No calcification*	*Percentage*
Simple aortitis	22	2	9	20	91
Simple dilatation	11	5	45	6	55
Aortic regurgitation (alone)	25	11	44	14	56
Aneurysm (alone)	22	11	50	11	50
Aortic regurgitation plus aneurysm	28	15	54	13	46

It seems that factors involved in the process of syphilitic aortic dilatation—possibly the destructive processes resulting from spirochætal activity—exert some influence in the laying down of calcium in the damaged aortic wall. Other factors, however, must play a considerable part in determining the degree to which calcium shall be deposited. There may possibly be some relationship in this respect with the quantity of circulating blood cholesterol (as is found frequently in atherosclerosis), or with the presence of small local thromboses in the aortic wall due to spirochætal activity, and possibly other more remote conditions such as disturbances in acid-base equilibrium, calcium metabolism or hormonal balance. No such relationships, however, have as yet been proved, and at the present time remain purely speculative.

In the light of our modern information on the subject of atherosclerosis, an excellent summary of which has been given by J. B. Firstbrook,[1] it seemed possible that that disease might play some part in the laying down of calcium in the syphilitic aorta. If that were so, and in view of the frequent association of atherosclerosis with hypertension, it would have been expected that there would be a higher "calcification rate" among the hypertensives than among the normotensives. In the present series, this has been shown not to be the case, as reference to the findings listed below will show.

When aortic regurgitation is present, there will naturally be a tendency for the diastolic pressure to remain low, so that the systolic pressure alone must be used as a standard in determining whether or not hypertension is present. Using a persistent systolic pressure of 160 mm./Hg. or more as a criterion for the presence of hypertension, it was found that 42 cases in the present series (of 108 cases) were hypertensive. Of these cases, 16 (38%) showed radiological evidence of calcification of the aorta. In contrast, 28 (42%) of the remaining 66 cases with no hypertension showed calcification. It is, of course, not known how many of these patients had suffered from hypertension at some previous stage of their disease.

If, on the other hand, the criterion for hypertension is taken as 150 systolic pressure, there is little change in the overall picture, 39% of the hypertensives and 39% of the normotensives showing calcification of the aorta.

In view of these findings, there does not appear to be any evidence to support the idea that hypertension *alone* plays any part in that train of events which leads to the deposition of calcium in the aorta. Since hypertension and atherosclerosis are so frequently associated together, the findings in this study would lead us to question the likelihood of atherosclerosis playing any major part in the calcification which occurs in syphilitic aortic disease.

Site of aneurysms.—There were 50 cases of aneurysm reported in the present series—with or without aortic regurgitation.

In 43 cases (86%) the aneurysms were situated in the ascending aorta, though in 28 of these the dilatation extended to a variable extent into the aortic arch. In 4 of these latter cases the actual aneurysm involved the arch as well as the ascending portion of the aorta.

In 4 cases the aortic arch was primarily involved, though the dilatation in these instances tended to spread into adjacent areas as is only to be expected when the aneurysm attains any considerable size. The aortic arch was therefore grossly involved in a total of 8 cases (16%)—four primarily, and four as an extension from aneurysms of the ascending portion.

In the remaining 3 cases the aneurysm involved primarily the descending aorta, though in these cases the dilatation was so extensive that the whole thoracic part of the vessel was involved to some extent, including the arch and the ascending portion.

Of the 43 cases in whom the aneurysm was situated in the ascending aorta, 28 (65%) suffered also from aortic regurgitation, while 15

(35%) showed no clinical evidence of this complication.

Only approximately two-thirds of these cases of aneurysm of the ascending aorta, therefore, were suffering with the additional complication of aortic regurgitation.

Concomitant disease.—In this series, there were 25 cases (23%) of concomitant neurosyphilis. This follows closely the average findings of other workers in this field. Arteriosclerotic changes and hypertension were of common occurrence, as was to be expected in persons of the age groups coming under review. Coronary heart disease, diagnosed clinically and confirmed electrocardiographically, was present in 20 of these patients during the period of observation, and myocardial infarction (autopsy finding) was the cause of death in 10. It is difficult to decide in how many patients coronary artery disease commenced as a relative insufficiency due to gross cardiac hypertrophy, though in some instances cardiac hypertrophy was not a marked feature. In some cases, at least, there was probably a primary atherosclerotic basis for their coronary disease.

Other changes associated with gross cardiac hypertrophy and failure were occasionally noted, including heart block, bundle branch block, extrasystoles, etc., and 5 cases in whom auricular fibrillation occurred.

Carcinoma was present in 3 patients in this study—all of the gastro-intestinal tract. Late syphilitic skin lesions were present in 3 cases and gastric ulcer in another 2. All these five patients were suffering, in addition, from neurosyphilis. This is interesting in view of the claims made by other workers[2] that gastric ulcers are considerably more common in patients suffering with neurosyphilis than in the general population.

Electrocardiographic changes.—There are no special changes in the electrocardiogram characteristic of syphilitic heart disease. When such changes occur, they should be regarded either as a measure of the myocardial embarrassment resulting from the mechanical strains and stresses put upon it by a mal-functioning aorta or aortic valve, or possibly as an indication of concomitant disease of a totally different nature, *e.g.*, coronary atherosclerosis, etc.

The electrocardiograph should be used, therefore, not as a means of diagnosis, but rather as an aid in assessing the state of the myocardium at the time of examination.

It should be emphasized that any changes in the heart which occur as a result of syphilitic involvement of the aorta are almost invariably the result of a mechanical defect and not of syphilitic involvement of the myocardium. It must also be borne in mind that the age at which cardiovascular syphilis is most frequently discovered is also the age when atherosclerosis reaches its highest incidence, and these two conditions not infrequently coexist in the same patient.

In view of these remarks, it must be understood that electrocardiographic changes, when they occur as a result of cardiovascular syphilis, are to be expected only in the late stages of the disease, when mechanical defects have become such as to cause serious embarrassment to the myocardium.

Coronary osteal occlusion, as a result of local inflammatory swelling, has been cited as a cause of death in certain instances, but this must be extremely rare. It might, conceivably, occur in the early acute inflammatory phase of the disease, but when gross dilatation of the aorta has occurred, the post mortem appearance is that of atrophy with stenosis rather than of any marked degree of swelling. It has been occasionally reported as a cause of death immediately following the commencement of active antisyphilitic treatment—possibly this could be the result of an acute local Herxheimer reaction.

The electrocardiographic findings in the present series of cases merely serve to confirm the remarks made above. Few changes were noted in those 22 patients with simple aortitis. One of these patients developed heart block and later died of myocardial infarction—the result of coronary atherosclerosis. Left axis deviation was present in most of those patients with well established cardiovascular changes, especially when associated with hypertension and cardiac hypertrophy, but in only a few of those with simple aortitis and aortic dilatation.

In advanced stages of syphilitic aortic disease various electrocardiographic patterns were seen —mainly the result of conduction defects, and of coronary insufficiency, relative or absolute. Superadded coronary atherosclerosis was present in a small proportion of this series, with associated electrocardiographic changes, and confirmed on post mortem examination.

Auricular fibrillation occurred in 5 patients, but this is not characteristically a finding due to syphilis, but rather to other myocardial condi-

tions which in these instances were associated with it. In one case, at least, there was good reason to suspect the co-existence of old rheumatic heart disease.

Prognosis.—The prognosis of syphilitic aortic disease depends upon a variety of factors, particularly the site and degree of maximum involvement, pressure of aneurysms on adjacent structures, the degree of mechanical embarrassment to the heart, the occupation of the patient, and the presence or absence of other conditions affecting the health and function of the myocardium.

If the condition is discovered before marked structural damage has occurred, and early adequate antisyphilitic treatment is instituted, there appears to be a reasonable hope of arresting the progress of the disease and its train of mechanical disasters. The effectiveness of penicillin in this stage is suggestive but will be by no means proved for another ten or twenty years.

Obviously, the treatment of choice is to cure the syphilis before any structural changes have occurred in the aorta. Failing this, the next choice is to abolish the infection before the damage has become too great. On the other hand, antisyphilitic treatment of a patient in whom a gross mechanical defect has occurred in the aortic valve, or in whom there are severe pressure symptoms from a large aneurysm, is not likely to achieve much in arresting the progress of the mechanical defect or in relieving the patient of his symptoms.

Reference to the following table will show the death rate in the present series of cases, according to the type and degree of aortic involvement.

TABLE V.

	No. of cases	*Observation average duration (years)*	*Died*	*% died*	*Duration of observation of those who died (years)*
Uncomplicated aortitis	22	1–11/12	2	9	Max. – 1 yr. Min. – 3 mos. Av. – 7½ mos.
Simple dilatation	11	3–3/12	0	0	—
Aortic regurgitation	25	2	9	36	Max. – 6-5/12 Min. – 2/12 Av. – 2-5/12
Aortic regurgitation plus aneurysm	28	2–7/12	8	29	Max. – 7 Min. – 2/12 Av. – 2-4/12
Aneurysm (alone)	22	2–6/12	13	59	Max. – 6-2/12 Min. – 2/12 Av. – 2-3/12

It will be seen that the death rate was high when gross structural changes had occurred, and that in an average of approximately two and a half years of diagnosis, over 30% of those with aortic regurgitation and over 40% of those with aneurysm had died.

It should be borne in mind, however, that these deaths are not all attributable to their syphilitic disease. As has been previously pointed out, these patients mostly are discovered in the age group when a high percentage of deaths occurs from atherosclerotic coronary artery disease and other causes. This may have a considerable influence in exaggerating the death rate of those suffering with syphilitic heart disease.

One patient in this series died of carcinoma of the pancreas, and another of cerebral hæmorrhage. Three are known to have died of myocardial infarction, and coronary disease was a complication of several others.

In many instances the patients have first reported on account of symptoms leading up to a terminal heart failure, and there was no way of knowing how long previously they had been suffering with their aortic disease. On the other hand, a young man of 28, who is suffering with congenital syphilis complicated for the last nine years by aortic regurgitation and a blood pressure which has now reached 200/0, is still alive and working periodically as a labourer.

Prognosis depends, therefore, to a considerable extent, upon many other complicating factors in an age group when physical disintegration from causes other than syphilis is steadily gathering momentum.

SUMMARY

A series of 108 consecutive cases of cardiovascular syphilis has been reviewed.

The cases were divided into five groups according to the stage and type of aortic involvement, and the groups discussed separately and compared as regards age incidence, duration of infection, symptoms and electrocardiographic changes, as well as the complicating factors of concomitant non-syphilitic disease.

Prognosis is discussed in relation to the stage and type of syphilitic involvement, and stress is laid upon the importance of taking into consideration the effects of non-syphilitic heart disease in modifying the assessment, prognosis and treatment of patients suffering with cardiovascular syphilis.

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COMMON PITFALLS IN MEDICAL PRACTICE

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TWENTY YEARS after graduation one should be in a position to look back over one's errors, and the errors of one's colleagues, with the hope of seeing them in proper perspective; freed from the emotional associations of their occurrence one may view them with desirable detachment. Having spent six of the twenty years in the Army in daily and intimate contact with the personalities and the work of medical confrères from every part of the country it is possible, perhaps, to speak of some of the errors and the pitfalls common to Canadian medicine as a whole.

In immediate preparation for this presentation I asked a number of my colleagues around the hospital lunch table what, in their opinion, were the commonest mistakes in medical practice. Interestingly enough, the most frequent single reply was that the commonest error lay in the taking of a poor history. This comment interested me greatly because it happened that I had been amusing myself with an experiment in the technique of teaching, enquiring into the effectiveness of the history and in particular the history of the present illness as an instrument of medical investigation. I am allotted four final-year students each month and spend a morning a week with them when each takes on the complete investigation of a new case. It is insisted that they follow a stereotyped form of history-taking and it has been most interesting to find that, provided they adhere closely to the outline given, these students are able, usually, to come to an adequate differential diagnosis within the first five minutes of seeing the patient. In the next twenty minutes, at the completion of the history of the present illness, they are confirmed in what usually turns out to be the correct diagnostic impression. A careful physical examination and the indicated laboratory study, although always insisted upon, only infrequently add new or important evidence. The history is a most important diagnostic device and, in my opinion, we make a mistake when we focus the students' attention upon its details rather than upon its purpose, because its diagnostic effectiveness is then lost sight of and it is often neglected.

There are certain diagnostic pitfalls in daily practice sufficiently often encountered to warrant consideration. One which caused a great deal of difficulty in the Army was the frequent failure to distinguish between the left submammary pain of anxiety and the true anginal pain of coronary insufficiency. If one's experience with junior medical officers from many parts of our country is any index of what occurs in Canadian medicine, then a very considerable number of people across our country are being wrongly labelled as having angina pectoris. Why is this error made? Coronary pain is rarely, if ever, at its maximum below the left nipple and it never has the darting, stabbing character of the effort syndrome pain. In cases of doubt the other features of anxiety and the irregularity of the pain's occurrence should give one the lead. A second error in cardiology frequently encountered in the Army was the undue attention attached to the finding of soft systolic murmurs at the cardiac apex. These were frequently found during the periodic examinations of troops, and the patients were sent up to the consulting clinics with the diagnosis of valvular disease of the heart. In the absence of other murmurs and with normal heart size and negative rheumatic history, a soft apical systolic murmur is of no significance, especially if it varies with the patient's respiration or position. Indeed, when one thinks of the physical turmoil in the heart during systole it seems strange that the turbulent, rushing blood does not always set up a perceptible sound!

Turning to another system, there are frequent errors made in overlooking hyperfunction or hypofunction of the thyroid gland. This may be the case where the dysfunction is mild or, under certain conditions, even severe, especially in older patients. One does not think of pain as an accompaniment of thyroid depression and yet I recall three patients with hypothyroidism in whom chest pain or back pain was the presenting complaint. In one the first clue to the diagnosis came with the low waves in an electrocardiograph taken because of a typical angina pectoris; the second was discovered when I finally had the wit to suspect there might be more than lumbago present; and in the third a colleague was able to explain a polyarticular pain by a low B.M.R. which I had missed and,

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incidentally, in all three, thyroid extract relieved the pain when other measures failed. Equally important are those cases with unsuspected, elevated basal metabolic rates. Older hyperthyroid patients may show few of the classical nervous manifestations. Loss of weight, tiredness and, indeed, the general manner and appearance of accelerated senile change may be the presenting features and it may only be on noting a rapid pulse that the underlying disease is suspected and a toxic thyroid nodule looked for.

Of the errors into which we fall in the diagnosis of the respiratory diseases a frequent one is the failure to consider the possibility of a virus pneumonia in the case with the unusually protracted "bad cold"; a chest film may be the only means of discovering the small and deeply-seated patch. It still happens, too, that the young person with the apical lesion visits his doctor several times because of unexplained fatigue, and the all-important "minimal" stage of his tuberculosis may be missed for the want of an early chest x-ray. Unbelievably, we still forget that early tuberculosis may be present without cough or pain in the chest.

Another tragic error, of which we have had more than one example admitted to the wards of the hospital I attend, has to do with the follow-up of the disease pneumonia. When the fever is gone and resolution is complete, most of these cases cease to be in need of further medical care. However, with the antibiotics we are now curing pneumonias previously incurable and among them the pneumonitis in the area of atelectasis peripheral to stenosing, carcinomatous lesions of bronchi. The infection in the collapsed lung used formerly to proceed to abscess formation but, now, it may respond promptly to antibiotics and, with its subsidence, the œdema of the bronchus at the site of the tumour lessens and an airway is re-established. With the lung tissue peripheral to the carcinoma returning to a condition approaching normal and the patient clinically well, can one be blamed for thinking that he has "cured" an ordinary "pneumonia"? It may only be when attention is drawn by persisting cough that the all-important follow-up x-ray is taken; and it may then be too late for lung surgery. I have in mind two such cases; at autopsy the first showed invasion of the pleura by carcinoma in a patient treated for a seemingly unremarkable pneumonia four months before. A follow-up x-ray of the chest was not taken until his admission to hospital. The second was a case of proved carcinoma of the lung, admitted for surgical assessment, in whom an extensive pneumonitis developed peripheral to the growth. When the pneumonia was treated with penicillin so striking were the x-ray and clinical improvement that the patient was used several times in ward discussions as an example of this particular medical pitfall. The moral is that all pneumonias in patients of carcinoma age are deserving of follow-up x-rays and especially so if the course is unusual or if cough persists.

Shortly after I started in practice a young boy was brought to me because of recurring asthma. I did a routine physical examination, including the usual check of his external genitals, and then proceeded to focus my attention upon the chest condition. It was not until some months later that chance led me to examine his genitals again when I discovered that what I had taken to be a normal external meatus was, in fact, a deep but blind dimple and the true opening, pinhead in size, lay below and proximally. The boy's stream was very small and bladder examination revealed trabeculation and a large diverticulum already present. Since that time I have been on the watch for the condition and by checking all cases with what I have learned to recognize as the characteristic "flat-topped" appearance of the corona, I have been able to pick up several in whom meatotomy has relieved obstruction and prevented uræmia. There are few opportunities in medicine to confer so much so easily!

An error in the diagnostics of hæmatology arises from the frequent use of liver extract injections as placebos or as a therapeutic test without having first established the diagnosis with certainty. Liver extract or Vitamin B_{12} are for the treatment of those anæmias resulting from an arrest in bone marrow red cell production at the macrocytic stage and, practically speaking, for none other. While it is always unwise to give a therapeutic agent without specific indication, the particular difficulty in this case is that should pernicious anæmia be in the process of developing, inadequate treatment may allow its insidious progress and lead to postero-lateral cord changes which might otherwise have been avoided. A few injections of liver extract have the further disadvantage of confusing the bone-marrow findings and the reticulocyte response should one wish later to look into the case more fully. Al-

together, unless one is sure that the case is one of pernicious anæmia or one of the other macrocytic anæmias, it would be better to use iron or even other kinds of vitamin B as the temporizing measure or as the placebo. One should think of liver extract as a specific form of treatment for a specific disease, not to be started until we are so sure of the diagnosis that we are prepared to commit the patient to a lifetime of injections. I realize that there are a few temporary macrocytic anæmias but in the main liver is used in pernicious anæmia and in that disease the specific hæmatinic need is lifelong.

Of our many sins, however, I believe most of us are most often at fault in the realm of the psychoneuroses. More patients suffer from one form or another of functional nervous disorder than from any other single cause and we use more phenobarbital than any other drug. The nervous, the depressed and the anxious patients fill the round of our days and yet, for all the tremendous experience with this clinical material that we and our predecessors have had, our results are still not impressive. A similar relapse rate in the realm of organic disease would not long be tolerated. The explanation is not far to seek. The patient who has "nervous indigestion" or "nervous headaches" or who has "exhausting fatigue", for which adequate organic explanation cannot be found, can, as a rule, expect scant attention from the busy practitioner. The time necessary for a complete psychiatric study is great and the procedure is an exhausting one; so, fobbed off with placebos, these patients go from doctor to doctor and from doctor to quack and back again. Actually, a considerable number of them are easy to treat and in a fairly fundamental way. A little extra time, a reassuringly careful physical examination, a mild sedative and, above all, the feeling that someone is taking an interest in their troubles, will do wonders for many; and, not infrequently, in the others, a few shrewd guesses by the doctor will discover the philandering or drinking husband or the domineering mother-in-law, the difficult boss or the impossible job. If the basic explanation is not readily forthcoming, however, and the case continues to haunt one's waiting-room, an hour some Saturday afternoon recording the events of the patient's childhood, home life, schooldays, social and domestic activities, paying particular attention to the successes and the failures, may give the answer.

Most psychiatry should be done by the patient's own doctor; all that is needed is time, interest and a knowledge of the things that go into making a normal person. We could all do with some instruction in the last-named, incidentally. I keep hoping that some day the psychiatrists will take time out from the ids, the egos and the sex lives and tell us what they've learned about the human emotions and how they grow. The students of the mind have accumulated a vast number of observations on the influences producing normal, adult and stable emotional apparatus and on the influences that retard and warp the mind in other directions. When our graduates are armed with this information they should be able, quite quickly, to decide which patients are those with deeply-rooted, basic defects of personality who will respond only to specialized and intensive treatment, and which are those whom they can care for themselves. And, also, how and at what point they should make such attacks. In the meantime, the rule-of-thumb diagnostic methods suggested above will often lead even such as you and I to the correct diagnosis and ultimately to the indicated psychotherapy.

In the foregoing I have dealt with the run-of-the-mill "nervous" patient. Our sins with them are chiefly those of omission and we shall do better as we learn more. The diagnostic problem of the psychotic or the prepsychotic individual, however, is a different and often much more urgent matter. The chronically tired patient with the somewhat bizarre complaints, who needs only to be asked a few questions for the correct diagnosis of an oncoming endogenous depression to be made, visits and eludes each of us at some time in our practising lives. And yet so little is required for a train of events to be set in motion whereby shock therapy and other psychotherapeutic measures can save him from prolonged disability and perhaps even from the suicide he may have in mind. To avoid error one must remember that endogenous depression masquerades as many things; that a common presenting feature is fatigue; and, if you listen for it, a bizarre quality often can be heard as an overtone running through the details of the history. The fatigue is often flat, dull and unconvincing and if one persists one discovers that it is not fatigue at all but loss of interest. The patient will admit he is depressed if you ask him. How depressed? Tears? So depressed that at times it

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hardly seems worthwhile carrying on? If under your tactful questioning he admits that he has thought of "doing something" to end his troubles you have a medical emergency on your hands. Get the patient to adequate psychiatric help as soon as you can. He may even now have the pistol in his pocket and if you fail him and send him away he may use it. And, incidentally, he may use it on you, too. My psychiatrist friends tell me that simple depressives are never homicidal but I have a feeling that the distinction between an endogenous depression and a depressed, paranoid schizophrenic would seem unnecessarily academic to my widow!

In these days we hear a great deal about the importance of the personal touch in the practice of medicine. The medical educationalist and the medical politician guiding the organized trends in our profession have isolated and are turning the full light of publicity on the usefulness of this factor. When one human being deals with another there are countless small interfaces of contact, many of them undefinable, many unrecognized, which lead the one to trust the other and have confidence in him. When we know more about the physiology of the emotions we may learn why confidence of the patient in his doctor is important, but for the present we can say that to dispel the tensions and apprehensions of the sick man and for the true evaluation of his story and for his successful treatment this element must be present.

If confidence is important whence does it come and how can it be developed? There are two things about patients which doctors should never forget. These are that patients have hopes and they have fears and when you strip their mental processes down to the things that matter most these are the elements you find. The sick man wants his doctor to be interested in him. He wants him to sense how pathetically he will grasp at what hope there may be and he hopes the doctor is aware how icy is fear. Students might well be taught to approach sick people saying this prayer, "Lord, let me not forget that this 'case' is a human being. He is sick. He is frightened—and he wishes he had something to be hopeful about!" Perhaps if this approach were hammered into us in those tender and unpreoccupied years there might be fewer tactless discussions at bedsides. And we might remember to give a little less attention to the scientific aspect of disease and a little more thought to the person who is the patient.

On one occasion following giving this paper I was asked, "What should one tell the patient in whom one has diagnosed fatal illness?" This is a very difficult question to answer. Should one tell him the truth; should one evade the issue; should one lie to him? There is no single reply to all these nor any certain course for all cases. However, after discussing this problem with my elders and on reviewing my own smaller experience, it seems to me that there are certain rules which may be followed as guides. It is generally accepted that the information should be given to someone in a position of responsibility in the family. This is a wise rule but it may sometimes prove inadequate, as happened in the case of the businessman who not having been told that his operation had been for a cancer of the stomach felt so well after discharge from hospital that, without consulting his family, he invested all his money in a new business venture. With his death a year later from carcinomatosis his dependents were left penniless. A second rule is that it is always wiser to speak the truth, although, of course, it is not always necessary to tell all one knows. I have come to the conclusion that there seems to be within many patients a protecting mechanism against things they do not want to hear. I assume it is the same means that protects the hysteric against his troubles and that allows you and me to forget the things we do not want to remember. To most people the news of death is unbearable and they evade it. They may hint at it and leave the way open for you to tell them the diagnosis but they do not press you for it.

There are other patients, however, who demand the truth. They are direct, certain and resolute in their inquiry and this protecting mechanism does not seem to function with them. When I am allowed to do so I answer these people straight-forwardly. I reason that they would not look me straight in the eye and ask the direct question if there were not something within them that called for the truth. How are we to know the innermost things of a man's mind? The patient who has always faced things may have derived his strength and his resolution from that approach towards life and perhaps that is the way he should die. I shall never forget a young couple of mine who asked for the truth and who went down their via dolorosa to-

gether, hand in hand, their heads up, each comforting the other. It was their finest hour and if I had not been honest when honesty was indicated, it would have been denied to them.

This paper deals with a few of the pitfalls along the way of a doctor's work. I have stumbled into quite a few of these at one time or another and although I have been encouraged to find how good my company has been, it is always a regrettable experience. May I close with this warning; where there are signposts they are poorly marked!

THE PRESENCE OF Q FEVER COMPLEMENT FIXING ANTIBODIES IN SERA OF INHABITANTS OF THE PROVINCE OF QUEBEC*

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Q FEVER INFECTION in humans occurs in many parts of the world. It was first discovered in Australia[1, 2] and later observed in both United States and Europe. Its presence in Canada, however, has not been investigated to date although the geographical and ecological conditions in this country are favourable to its propagation. The authors have therefore conducted a preliminary investigation in Quebec testing the sera of a number of residents to look for the presence of Q fever antibodies.

Technique.—The specimens of serum were taken from people living in Montreal and Chicoutimi, Que. and the Kolmer-Boerner technique for complement fixation with overnight-ice-box incubation was used. The antigen chosen was the Q fever diagnostic antigen prepared by Lederle from Nine Mile American strain.

Results.—Out of 218 samples of human sera examined, 10 (4.6%) were found to contain specific antibodies for Q fever with titres 1:32 and more; 23 (10.5%) titred between 1:8 and 1:16 and 27 (12.4%) titred 1:4 (Table I). The highest titres recorded were 1:128 and 1:256. These sera were taken from two young girls, 13 and 3 years old. And it is interesting to note that from male subjects more positive sera were obtained from those under 15 years of age (14 cases) than from adults (3 cases) (Table II). These preliminary figures suggest that the number of positive sera is greatest among the younger members of population and decreases in older subjects.

TABLE I.

Age	*Number*	*1/4*	*1/8*	*1/16*	*1/32*	*1/64*	*1/128*	*1/256*	*Percentage*	
									1/8 – 1/16	*1/32–*
1 -5	31	3	—	7	1	—	—	1	22.6	6.4
6 -10.....	42	6	5	1	3	—	—	—	14.3	7.1
11-15.....	28	3	2	—	—	1	1	—	7.1	7.1
16-25.....	26	4	3	—	—	1	—	—	11.5	3.8
26-70.....	91	11	3	2	2	—	—	—	5.5	2.2
Total.....	218	27	13	10	6	2	1	1	10.5	4.6

TABLE II.

Sex	*Age*	*Number*	*1/4*	*1/8 – 1/16*	*1/32–*	*Percentage*		
						1/4	*1/8 – 1/16*	*1/32*
M.	1–15	65	9	9	5	13.8	13.8	7.7
	16–70	59	8	2	1	13.6	3.4	1.7
	Total:	124	17	11	6	13.7	9.7	4.8
	Age	*Number*	*1/4*	*1/8 – 1/16*	*1/32–*	*Percentage*		
						1/4	*1/8 – 1/16*	*1/32–*
F.	1–15	36	3	6	2	8.3	16.6	5.5
	16–70	58	7	6	2	12.0	10.3	3.4
	Total:	94	10	12	4	10.6	12.7	4.25

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DISCUSSION

Bengtson,[3, 4] and Beck and his collaborators,[5] have proved that complement fixing antibodies which appear in the sera of patients with Q fever are specific and persist for a long time after convalescence. Therefore, to check the specificity of our results, we have repeated the complement-fixation reaction of some positive sera using three other rickettsial antigens: Q fever Italian strain (Henzerling), Rocky Mountain spotted fever, and epidemic typhus fever. Out of 27 sera thus retested with the Italian strain, we found only 4 showing higher titre with the Italian strain than with the American strain. And this difference was of only one tube using two-fold dilutions. 6 sera had the same titre with both antigens and 17 gave higher titre with the American's strain. Out of 24 sera tested with the Rocky Mountain spotted fever antigen we found only 4 which reacted positively in 1:8 and 4 in 1:4. These titres with Rocky Mountain spotted fever antigen were always lower than those with the Q fever antigen. No serum positive for epidemic typhus fever was found.

These results lend weight to our belief that Q fever is present in the Province of Quebec even though the disease has not yet been diagnosed nor the virus isolated.

CONCLUSIONS

1. The presence of a significant level of Q fever antibodies in the sera examined suggests that this disease is present in the Province of Quebec.

2. 4.6% of the residents of Quebec examined had Q fever antibodies with a high titre (1:32 and more) and 10.5% (considered as doubtful) showed titres of 1:8 and 1:16.

3. A greater number of positive sera was found in children than in adults. This points to infection at an early age.

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ISLET CELL TUMOURS OF THE PANCREAS*

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MY APPRECIATION of the honour of being asked to deliver the Banting Memorial Lecture is indeed honest and sincere. But great as is my appreciation, it is accompanied by a sense of my temerity as a surgeon, in attempting to do justice to the accomplishments of the Toronto group of scientists in discovering, developing and perfecting the hormone "insulin" that, the world over, has meant so much to so many. It is my interest and experience in islet cell tumours, the understanding of which was a direct result of the discovery of insulin, that has induced me to appear before you.

In discussing this subject of islet cell tumours and hyperinsulinism, it is appropriate to introduce some of the historical background of pancreatic research to explain the slow progress in understanding the endocrine function of that deep-seated but important organ.

The pancreas is one of the few organs that has both internal and external secretions. The stomach, the testes, the ovaries, and probably the liver and the kidney have this double function. As in the other organs mentioned, the exocrine function of the pancreas was studied and understood before the endocrine function was even suspected.

In 1890, von Mehring and Minkowski[1] published their studies on the complete removal of the pancreas with resultant symptoms closely resembling those seen in human diabetics. Ever since von Brunner[2] in 1682 stated that removal of the pancreas in dogs produced no ill effects, other experimenters had incompletely extirpated the pancreas without causing diabetes. But it was Minkowski especially who deserves the credit for establishing the fact that complete pancreatectomy results in diabetes, for he[3] independently demonstrated it in 1892. He implanted a portion of the pancreas beneath the skin of dogs and allowed them to remain until the circulation was established. When the remainder of the gland was removed from the abdomen, diabetes did not appear. But when the pancreatic graft was removed the dog became diabetic. He correctly deduced that the diabetic symptoms were caused by a lack of some specific function. De Dominicis,[4] in 1891, independently made similar observations in depancreatized animals. And Lepine[5] in 1893, repeating these experiments, was the first to advance the theory that the pancreas elaborated an internal secretion which controlled carbohydrate metabolism.

Although Langerhans,[6] in 1869, was the first to describe the morphology of the islet cells, as distinct from the acinar cells, he did not express an opinion as to their function. He made these histological studies while

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still a medical student in the University of Berlin. Diamare[7] in 1889, showed that in certain of the teleosts (cod, haddock, flounder and sculpin) the islet tissue exists separately from the acinar tissue. He and Laguesse,[8] in 1893, were probably the first to suggest that islet tissue is active in the production of an internal secretion that has to do with the control of carbohydrate metabolism.

A number of investigators, including Ssobelow[9] had ligated pancreatic ducts producing atrophy of the acinar tissue and leaving normal-appearing islet tissue in non-diabetic animals. It remained for Ssobelow to make and record a most significant observation. He said; "The future will show how far experiments in this direction will be crowned with success. Even now we may come nearer to the solution of the problem by making exact studies of the islands *in vitro* and *in vivo*. Formerly the entire pancreas was used for this purpose. Now, however, by ligating the excretory duct, we have a means of isolating the islands anatomically and of studying the chemistry of these cells separated from the digestive ferments.

"This anatomic isolation of the islet cells enables us also to try organotherapy in diabetes in a rational manner. All former attempts to cure diabetes by administering the whole pancreas in various ways have failed. Since it is difficult to secure in any quantity pancreas in which only the islet tissue has been preserved, one can substitute pancreas of newborn animals—calves for instance, in which the islands are well developed in comparison to the digestive apparatus. Moreover, the pancreas of the newborn is little capable of digestive activity and we may expect that its digestive juice will not interfere with the action of the substances secreted by the islands. At all events, we are justified in the hope that in the near future, the question will be decided whether or not this method of approach will succeed in relieving the ills of the diabetic patient."

This prophetic statement was made in 1900, more than twenty years before the established discovery of insulin. It is astonishing how many investigators came so near the discovery—a number produced a substance which controlled the glycosuria and hyperglycæmia in diabetic animals and even in human diabetics, but misinterpreted the results or attributed them to wrong theories.

Following Minkowski's[10] published inconclusive results in experiments in which he injected pancreatic extracts into depancreatized dogs, alleviation of the symptoms in depancreatized dogs or in a diabetic patient by the administration of a pancreatic extract was established as the criterion of therapeutic activity. Numerous attempts to accomplish this result were frustrated by the use of the entire pancreas in making the extract, or by the administration of extracts obtained from islet tissue by the oral route. Gley[11] used pancreas that had the acinar tissue sclerosed by duct ligation and found that intravenous injections of such extracts were capable of reducing the sugar in the urine of diabetic dogs. In 1922, after the discovery of insulin, he[11] asked that a communication that he had deposited in 1905 at the Société de Biologie be opened and read at the meeting of the society held in Paris on December 23, 1922. In this communication, Gley stated that diabetes mellitus was probably caused by a dysfunction of islet tissue. He said that he had prepared extracts from the pancreas in which acinar tissue had been sclerosed and had found that in depancreatized dogs glycosuria was considerably diminished. Because of his work in other research problems, he had not continued his investigation of this pancreatic extract.

In 1907, Zuelzer[12] and his associates prepared a pancreatic extract by ligating the pancreatic veins of recently fed calves and an hour later excising the pancreas, mincing it and treating the material with alcohol. They injected this material, supposedly freed of its protein content, into depancreatized dogs and into eight diabetic patients. Their protocols showed a reduction in glycosuria and a removal of ketone bodies in the human subjects after intravenous injection of the extract. But their injections caused chills and temperature, and this febrile reaction was mistakenly considered to be the causative factor, rather than a specific hormone. For this reason, the use of the extract was discontinued. The febrile reactions were no doubt due to foreign protein reaction or other impurities in the potent extract which Zuelzer undoubtedly had prepared. Scott[13] in 1912, used 90% alcohol to extract the antidiabetic hormone from the pancreas and to free it from digestive enzymes. When injected intravenously into depancreatized diabetic dogs, glycosuria was temporarily reduced. This effect was again misinterpreted by Scott. There is no doubt that a number of these earlier investigators were on the very brink of the conclusive proof of the antidiabetic hormone of the pancreas, but due either to oral administration or to toxic reactions with intravenous use or to overdosage, failed to discover the active hormone.

It remained for the remarkable group of Toronto investigators to startle an awaiting world by the announcement[14] in 1922 of their epoch-making discovery.

Sigerist[15] in the first volume of his monumental *History of Medicine*, now being published, discusses the factors of Time and Space in determining the accomplishments and fame of the great figures in medicine. He says:

"Nobody will deny the great significance of the part played by the individual in the making of medical history, but we should also remember that the individual is to a large extent the product of his environment. . . . Even if we do not accept Hippolyte Taine's theories integrally, we must admit that the point at which a man lived in space and time, the environment and the historical moment are of extraordinary importance."

But time and space did not deter Frederick Banting from pursuing his determined course. His experience as a surgical intern in the Children's Hospital of the University of Toronto, in treating diabetic children, had left an indelible impression of the inevitable tragedy of diabetes mellitus in its attack on the younger generation. When he went to the University of Western Ontario in London, Ontario, to practice and later to work as demonstrator in physiology, this problem of the relation of the pancreas to diabetes was uppermost in his mind. His[16] own account of this interest in the problem is authoritative.

"On October 30, 1920, I was preparing a lecture on the relation of the pancreas to diabetes, and when the lecture was finished, I commenced the perusal of the newly arrived November number of the *Journal of Surgery, Gynæcology and Obstetrics*. This journal contained an article by Moses Barron[17] in which he pointed out the analogy between the degrenerative changes which follow the experimental ligation of the pancreatic duct and blockage of the duct by gall stones. After reading the article by Barron, I was unable to sleep. There seemed to be, in some vague way, a relation between the islet cells of the pancreas and clinical diabetes. There seemed also to be a means of attacking the problem of extracting the islet cells by ligating the pancreatic duct. It was not until two o'clock in the morning that I was able to crystallize the idea into a form that would lend itself to experimentation. At this hour, I arose and wrote

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in my notebook the following words "Ligate pancreatic ducts of dogs. Wait six to eight weeks for degeneration. Remove the residue and extract."

This note which he made then was, and continued to be, his thesis, and succinctly defined his purpose and his project. Even had he been fully aware of the unsuccessful investigations along the same lines by earlier workers, I do not believe he would have been deterred from his purpose, any more than by the discouraging advice which the physiologists whom he consulted gave him.

Of course the story of his coming to work in the physiological laboratory of the University of Toronto is familiar to all of you. To my mind, the most fortunate happening for Banting as he began his work, was the assignment of Charles H. Best to co-operate with him in his project. It was Banting's persistent determination and his clear conviction that he had a worthwhile idea that transcended the failures of earlier investigators and his discouragements before he began his project. To him belongs the credit of initiating the experiments leading to the discovery of insulin. But to both Banting and Best belongs the credit of conducting the experiments, and to J. B. Collip for his work in purifying insulin so that it could be used clinically in the treatment of diabetics by Campbell and Fletcher.

Finally, it was the co-operation of the laboratory and clinical groups in the University of Toronto, the Toronto General Hospital and the physicians in different medical centres of the continent, experienced in the treatment of diabetics that resulted in the demonstration of the efficacy of insulin as a therapeutic means of controlling the diabetic state and its world-wide acceptance.

Following the discovery of insulin, Macleod[28] in 1922, published his studies in teleosts, whose islets are anatomically distinct from acinar tissue. He definitely established the fact that insulin is elaborated only by islet tissue. Acid alcohol extraction of islets in these fish yielded large amounts of insulin, whereas acinar tissue similarly treated yielded none.

Following the discovery of insulin and the establishment of its effectiveness in the treatment of diabetes, Campbell, Fletcher and other clinicians in the University of Toronto found that overdosage of insulin resulted in abnormal nervous manifestations, varying with the amount of insulin given and in the individual patient, from mild symptoms of weakness, anxiety, and vasomotor disturbances to mental depression or excitement, to delirium, unconsciousness and even coma. Dr. Seale Harris of Birmingham, Alabama, had been selected by the Toronto group as one of the clinicians experienced in the treatment of diabetes, to study the effect of insulin on the blood sugar levels and glycosuria. He began to use insulin in January, 1923. Because of the reactions he noted, he decided to visit Toronto to get more information from Banting and Best and the clinicians using insulin. In March, 1923, he spent a week with the Toronto group, and had the opportunity of studying a number of diabetics with insulin reactions of varying degrees. I quote from Dr. Harris:[18]

"One morning after going the rounds with Dr. Banting in the diabetic wards of the Toronto General Hospital, in discussing insulin reactions, I said to him 'Since you have proved that diabetes is due to deficient secretion of insulin by the pancreas, it seems there should be the opposite condition, in which the pancreas secretes too much insulin, and if so, the spontaneous excessive secretion of insulin in an individual should produce the same symptoms observed in diabetics from overdoses of insulin. Furthermore, I am sure that I have seen patients who did not have diabetes and had not used insulin, who have had the same symptoms that we have observed in diabetics from overdoses of insulin.' Dr. Banting replied that he had seen nothing in the literature suggesting a disease due to spontaneous excessive secretion of insulin, and it had not occurred to him that overfunction of the islet cells of the pancreas could cause an opposite condition to diabetes."

Within a week after his return from Toronto, Dr. Harris was consulted by a physician who gave a story typical of hyperinsulinism—a term suggested by Dr. Harris. This patient's blood sugar showed 65 mgm./100 and his symptoms were promptly relieved by drinking a solution of corn syrup.

By June 1924, Dr. Harris had studied five non-diabetic patients with symptoms of hyperinsulinism with hypoglycæmia, and he[20] reported them in a paper entitled "Hyperinsulinism and Dysinsulinism" at the meeting of the American Medical Association in Chicago in June 1924. Parker and Finley[19] had published a paper in May 1924 giving the results of treating ten non-diabetic patients with severe nervous manifestations, and stated that they were impressed with the similarity of these cases to patients having insulin hypoglycæmia. However, inasmuch as Harris had studied one of his cases even earlier than 1923, and had discussed his hypothesis with Banting in March of that year, the credit for discovering the entity of hyperinsulinism, defining it and naming it should go to him.

Hyperinsulinism, in different grades, is mani-

fested by as great a variety of nervous symptoms as are seen in patients with varying overdosages of insulin. This syndrome may be divided into three categories: the functional; the secondary, caused by dysfunction of other endocrine glands —notably the pituitary, the adrenal and the thyroid—and by certain hepatic lesions; and finally the type caused by functioning tumours of the islet tissue of the pancreas. Hyperinsulinism caused by functional islet cell tumours differs from the other two varieties for two reasons: (1) the hypoglycæmia in the fasting state caused by the hyperinsulinism is severe, below 50 mgm. %, in practically all the cases; (2) the only curative therapy is surgical. My discussion of this subject is based largely on a personal experience in the study and surgical treatment of 39 patients.

Incidence of islet cell tumours.—The incidence of this type of neoplasm is difficult to give statistically. In the past, before the discovery of insulin, these tumours were undoubtedly overlooked. The first pathological description of this type was by Nicolls[21] of Boston in 1902, but he gave no clinical record of his case. Even as late as 1926, Warren[22] was able to find only 20 cases, four of them his own, and he did not attach any physiological significance to them. But since Wilder[23] and his associates reported the first example of a carcinoma of islet tissue with fatal hypoglycæmia in 1927, and since the first successful removal of an adenoma of islet tissue was appropriately carried out here in Toronto, in 1929, by the late Roscoe Graham,[24] there have been reported over 400[25] islet cell tumours. Of 363 localized tumours, 161 were found at autopsy and 202 were removed by surgeons. This is rather a sad commentary on the care with which pathologists examined the pancreas prior to 1927 in their autopsies. However, these tumours are usually small, seldom exceeding 1.5 cm. in diameter, and can be easily overlooked unless serial sections are made of the pancreas. It may be said in extenuation of this discrepancy that the knowledge of the hypoglycæmic syndrome has made the pathologists more careful in their examination of the pancreas. Furthermore, some of these tumours may be non-functional and give no history of hypoglycæmia.

Pathology.—In general it may be said that four pathological changes have been described in the islands of Langerhans with severe hypoglycæmia. The first of these is diffuse hyperplasia of the islands. This is seen in some infants born of diabetic mothers, and dying of convulsions or coma with low blood sugars. As a result of supplying the diabetic mother during fetal life, some of the infants when born have hyperinsulinism with hyperplastic islet tissue. This hyperplasia is also seen in some patients with hypoglycæmia in the form of an adenomatosis of islet tissue as described by Frantz.[26] The other three pathological changes are seen in the benign adenomas, the questionably malignant adenomas,[27] and fortunately the less frequently found carcinomas with metastases. Furthermore, it must be said that a certain number of all these pathological entities are non-functional, in that they are not accompanied by over-production of insulin. However, in general it is true that the incidence of severe hypoglycæmia increases with the carcinomatous features of the tumours. It is also true that recurrence of hyperinsulinism is more apt to take place in the diffuse adenomatosis and the questionably malignant type of adenomas than in the encapsulated single adenomas. Of course, the true carcinomas with metastases are not cured by any known measure.

In our own series of 39 patients explored, we found 43 tumours: 27 adenomas, 3 adenomates, 9 questionably malignant, 4 carcinomas, one of them non-functional.

In the collected cases reported by Howard *et al.*,[25] there were 398 patients with islet cell tumours. There were 361 localized tumours. Of these, 313 were benign adenomas, 48 were classed as morphologically malignant but were clinically benign, the questionably malignant type. There were 37 carcinomas, 15 non-functioning. The incidence of multiple adenomas was 12.6%. These localized tumours are found more often in the tail of the pancreas, almost as frequently in the head, and somewhat less frequently in the body.

The great majority of adenomas are not large, averaging 1.5 cm. in diameter. They have a firmer consistency than the surrounding normal pancreas, and because of their extensive capillary network, they have a pinkish or pinkish-violet colour as compared to the ivory-coloured pancreas. They are most difficult to find if situated in the central part of the head. Palpation is the surest way of finding them, but in order to examine all parts of the organ, the pancreas has to be partially mobilized by dividing the peritoneum at the lower border of the organ and along the right margin of the duodenum.

Adenomas are readily enucleated from the surrounding pancreatic tissue. The true carcinomas are infiltrating, invasive growths. The adenomatoses give an indurated feel and require partial pancreatectomy.

Abnormal physiology in hyperinsulinism.—Although the exact function of insulin has not as yet been defined, we do know that it has a specific action in lowering the circulating blood sugar. That functioning islet cell tumours secrete insulin in excessive amounts has been proved by bioassays in rabbits and other animals. Furthermore, the nervous manifestations of patients with islet cell tumours during their "attacks" are clinically and biochemically indistinguishable from those seen in patients following overdosages of insulin, and lastly, removal of benign adenomas cures the patients.

That the brain is dependent upon the maintenance of an adequate supply of glucose and oxygen has been shown by Himmrich[29] and his associates in the study of schizophrenic patients in insulin shock. It was found that the average arterio-venous oxygen difference before insulin was given was 6.8 vol. %. At the time the patients lost contact with their surroundings, the reading was 2.6 vol. %, and when deeply comatose the reading was 1.8. These studies would indicate that the symptoms of hypoglycæmia are the result of decreased brain metabolism of glucose, and that the higher centres in the brain are the first to be affected. These higher centres of correlation and association are dependent upon a constant blood flow containing normal amounts of oxygen and glucose. Their blood supply is greater than any other area of white matter. The phylogenetically newer centres of the brain receive proportionately the largest amount of blood; they are provided with a greater amount of oxygen and glucose than other areas.

Recovery from the hypoglycæmia syndrome is brought about immediately on the administration of intravenous glucose. Spontaneous but slow recovery occurs in the majority of patients. This is believed to be the result of stimulation of the adrenals with an output of adrenalin in sufficient amounts to mobilize glycogen to be converted into blood sugar. Administration of adrenalin has been shown by Gammon and Tennery[30] to be effective in relieving the hypoglycæmic attack.

The electroencephalogram is being used increasingly in the study and diagnosis of islet cell tumours. The normal alpha rhythm of 8 to 10 cycles per second decreases as hypoglycæmia develops, reaching 3 cycles or less as coma intervenes. Administration of intravenous glucose quickly restores normal rhythm. This gives further evidence of disturbed brain metabolism, the result of hypoglycæmia. Repeated and prolonged attacks result in permanent functional disturbances of the higher cerebral centres in some patients, especially if the syndrome develops in the early age group.

Symptomatology. — The clinical picture of hyperinsulinism and hypoglycæmia is that of chronic disease characterized by periodic attacks of nervous disorders coming on at irregular intervals. Characteristically, the attacks occur during the fasting period or after severe exertion. They are relieved promptly on the administration of glucose solutions.

The symptoms of this syndrome are of course as various and variable as those caused by overdosage of insulin. They were first adequately defined by Wilder,[31] who was the first to describe a case of functional islet cell tumour[23] three years after Harris[20] had postulated the syndrome. Wilder divided the symptoms of the attacks into three categories: Those due to disturbances of the vegetative nervous system–restlessness, pallor, sweating, nausea, salivation; (2) those due to disturbances of the central nervous system—tonic and clonic spasms, uncontrolled motor activity, opisthotonus; and (3) those due to disturbances of the higher psychic centres—confusion, anxiety, loss of consciousness and coma. All of these are associated with varying degrees of hypoglycæmia.

Usually the patient follows the same individual pattern during subsequent attacks. It is interesting that the severity of symptoms does not necessarily correspond to the degree of hypoglycæmia in different individuals or at different times in the same individual; nor does the size of the tumour determine the severity of the symptoms. However, as previously stated, the carcinomas and the questionably malignant tumours usually show lower blood sugars and more frequent and severe attacks.

Differential diagnosis. — Inasmuch as hyperinsulinism and hypoglycæmia are found in conditions other than islet cell tumours, it is most important to rule out such conditions before considering the possibility of an islet cell tumour

and advising surgery. The functional types do not have as low blood sugars and respond to dietary measures. Hypoglycæmia due to dysfunctions of the pituitary should be ruled out by radiographic studies of the sella tursica and the visual fields. Adrenal disturbances are usually proved by their clinical and biochemical findings. Associated hyperthyroidism is seen in islet cell tumours, but does not give as high basal metabolism rates as are found in uncomplicated Graves' disease. For this reason, patients meeting the criteria of islet cell tumours with any elevation of the BMR should be given a preliminary course of iodine therapy. If this is not done, the patient may develop a postoperative thyroid storm, as did one of our adenoma cases with a fatal outcome.

Our experience in our own patients and in reviewing the reports from other clinics convinced us that true functional islet cell tumours showed fasting blood sugar levels below the 50 mgm. %, provided the test was done during a 24 hour fasting period or at the time of the hypoglycæmic attack. For this reason we gave up the use of the ordinary glucose tolerance test and used the 24 hour fasting blood sugar test. We adhered strictly to what we have called the essential triad in making the differential diagnosis. The triad requires: (1) that the patient must develop the hypoglycæmic attack during the fasting state; (2) twenty-four hour fasting blood sugar levels below 50 mgm. %, or below 50 mgm. % at the beginning of or during an attack must be demonstrated; (3) immediate recovery from the attack on administration of intravenous glucose.

If in addition to this triad, electroencephalographic studies showed a typical reduction of the normal alpha rhythm, we considered the diagnosis of islet cell tumour established, and advised surgery. By adhering to these criteria, we were able to prove the presence of and remove a tumour or tumours in 34 of 39 patients explored, 87%. Furthermore, we found a tumour in seven patients previously unsuccessfully explored.

TREATMENT

The only curative therapy for the most frequently found benign adenoma of islet tissue is surgical. There are three important reasons for not deferring surgery, once the differential diagnosis has been established. (1) Prolonged and repeated hypoglycæmic attacks may cause permanent cerebral degeneration and mental damage, even through the removal of the tumour of long standing cures the hypoglycæmia. (2) Certain of the questionably malignant adenomas and the adenomatoses become malignant later. (3) The prolonged increased carbohydrate intake necessary to control hypoglycæmia attacks results in excessive obesity and makes the surgery in the delayed cases exceedingly difficult for the surgeon and hazardous for the patient.

Preoperative care. — A 5% glucose infusion normal saline should be started an hour before operation and given slowly during the first half of the procedure.

Anæsthesia.—Either general or spinal anæsthesia given by an experienced anæsthetist, to provide adequate relaxation, is essential.

Incision.—The transverse supra-umbilical incision through both recti gives far better exposure than the split left rectus incision and greatly facilitates the exploration.

Procedure.—It is essential to explore every part of the pancreas to insure the finding of the tumour or tumours, for in 12% of the cases more than one tumour is found. To be sure of exploring the head of the pancreas, it is essential to mobilize it and the duodenum by incising the peritoneum to the right of the duodenum, so that the head can be palpated by the thumb and fingers of the left hand. Encapsulated adenomas can usually be readily enucleated and, unless persistent oozing continues, drainage is not indicated. Drainage should be used if a partial resection is done.

In certain cases of adenomatosis giving the essential triad, a definite tumour cannot be palpated. The surgeon is then justified in resecting the tail and body of the pancreas up to the superior mesenteric vessels, for the adenomatous tissue is much more apt to be found in the distal half of the pancreas. Fine silk suture and ligature technique throughout is to be preferred to catgut technique.[32]

That the tumour or tumours are easily overlooked by inadequate exposure and palpation is shown in the collective review[25] of 398 patients with islet cell tumours. In 118 patients, no tumour was located at the first exploration. Thirty-seven of these patients were found eventually to have a tumour; 12 having the adenoma resected blindly during subtotal resection of the pancreas; 12 having the tumour removed at a subsequent operation; and 13 having

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the tumour discovered at autopsy. In our own series of 39 patients, we found an adenoma in 7 patients previously explored.

RESULTS

In any form of therapy, it is the results that count and determine its rationale. In the collected review[25] of islet cell tumours reported in the literature, operative removal of the tumour consisted in exploration and enucleation in 153 patients and exploration and partial resection of the pancreas in 48 patients. The operative mortality of each type of procedure was about 9%. End results reported in the survivors were good in 87.3%.

In our own series of 39 patients, tumour or tumours were found in 34. There were five postoperative deaths in patients with tumour, and

TABLE I.

RESULTS IN ISLET CELL OPERATIONS
Postoperative deaths—7

2 Carcinomas
1 Pneumonia 4th p.o. day.
1 Hepatic failure, cirrhosis 10th p.o. day.
2 Adenomas
1 Thyroid storm 2nd p.o. day.
1 Partial pancreatectomy. Hæmorrhage 14th p.o. day.
1 Adenomatosis
Recurrent after 3 yrs. Partial pancreatectomy. Died cardiac failure 4th p.o. day.
1 Exploratory
Von Gehrke's disease. Hepatic failure 4th day.
1 Exploratory
Overdose of insulin 12 hrs. postop.

two in patients explored on wrong and dubious diagnosis with no tumour found, one a girl of 13 with von Gehrke's disease, the second a patient explored in coma with blood sugar levels of 20. It was found later that the patient had been given an overdose of insulin by a psychopathic nurse. Of the 32 survivors, all have been followed from 2 to 18 years (see Tables). The longest follow-up result is in Dr. Roscoe Graham's first patient, cured 22 years.

In closing I should like to emphasize that the diagnosis of islet cell tumours is not difficult if the essential triad is used in the differential diagnosis, and that in the benign tumours the results of operation are brilliant, provided the patient has not had the lesion for prolonged periods and provided a tumour other than the one removed is not overlooked.

SUMMARY

1. Islet cell tumours are predominantly functional, but both the benign and malignant in a few instances do not cause hyperinsulinism.

2. The functional islet cell tumours may be divided pathologically into four groups; benign adenomas (the most frequently found); questionably malignant; adenomatoses and unquestionable carcinomas with metastatic spread.

3. The benign adenomas may be multiple. For this reason, if one is found the rest of the pancreas must be carefully searched for other tumours.

4. In the order of frequency, benign adenomas are found in the tail, the head, and the body of the pancreas.

TABLE II.

POSTOPERATIVE FOLLOWUP RESULTS

Adenomas
10 patients followed 10-18 years } all relieved of their
7 patients followed 5-9 years } hypoglycæmic symp-
3 patients followed 2-4 years } toms
2 patients are in mental institutions. Hypoglycæmia cured.
1 patient died 2 yrs. postop. Duodenal hæmorrhage. Hypoglycæmia cured.
1 patient died 5 yrs. postop. Intestinal hæmorrhage. Hypoglycæmia cured.
Questionably malignant adenomas
5 patients followed 13, 9, 8, 8, 6 years. Hypoglycæmia cured.
1 patient hypoglycæmia recurred after 8 years.
Adenomatosis
1 patient free of hypoglycæmia 8 years.
1 patient free of hypoglycæmia 3 years, then recurred.
Carcinoma
1 patient died 4 mos. after exploratory in another hospital.
Patients explored—no tumour found
In 2 patients, symptoms continued. Tumour found in 1 patient 3 years later in another hospital. Suicide by 1 patient 4 mos. after exploration.
In one, symptoms relieved after partial pancreatectomy.

TABLE III.

ISLET CELL TUMOURS

Patients explored		39
Operations		44
Simple excision of tumour	21	
Partial pancreatectomy	10	
Reoperation—tumour found	7	
Pancreaduodenectomy	1	
Failure to find tumour	5	
		44
Adenoma	27	
Carcinoma (1 nonfunctional)	4	
Questionably malignant	9	
Adenomatosis	3	
	43	

Tumours found in 34 patients—87 per cent.

5. To find these adenomas, especially those in the head, the pancreas must be mobilized by dividing its peritoneal attachments so that the firm nodular masses can be adequately palpated and detected.

6. Benign adenomas, once removed, give immediate and permanent recovery from the hypoglycæmic state. However, if the tumours have existed for long periods, permanent cerebral damage from repeated hypoglycæmic attacks may result, although the hyperinsulinism is cured.

7. Recurrent hyperinsulinism as a result of recurrent or new islet cell tumours is more apt to occur in patients with multiple adenomas, questionably malignant tumours, and adenomatosis found at the first operation.

Finally, the following comments are offered relative to islet cell tumours and insulin.

1. In our work at the Presbyterian Hospital, numerous tissue cultures from the freshly removed islet cell tumours were made and studied by Dr. Marjorie Murray. These cultures grew readily and vigorously. These cultures also grew in the serum of the patient from whom the tumour had been removed. In four instances, the tissue cultures were gradually transferred from the donor's serum to mixed serum of a diabetic to the diabetic's serum. These grew readily in the diabetic serum but when these tissue cultures were implanted in the axillæ and groins of the diabetic patient, there was no decrease in the insulin demand of the diabetic and no evidence of persistence of growth in the transferred tissue cultures, over a period of weeks.

2. Not all congenital malformations are the result of changes in the germ plasm or genetically determined or hereditary. During the past decade, there has been an accumulating evidence that extraneous factors, such as contraction of measles by the mother early in pregnancy, may result in embryonic anomalies such as cataract and deaf mutism.

Last year, Dr. P. K. Duraiswami,[33] F.R.C.S., Research Fellow in the Department of Orthopædic Surgery in the University of Liverpool, published his very interesting experiments with insulin injected into the yolk of the eggs of developing chick embryos. In this report, carefully documented with x-ray films and pathological sections, he describes the malformations and skeletal abnormalities in cartilaginous bones that follow insulin injections at different periods of development. The hypoglycæmia thus produced deprives the cartilaginous skeleton and the eyes of the mucoprotein essential to the growth of these structures. Given at various periods, the following deformities occurred: 1st and 2nd day, vertebral column; 3rd day, claws and feet; 4th and 5th day, limbs and beak; 6th day, dislocation of hips; 3rd to 6th day in large doses, generalized osteogenesis imperfecta.

Broadly speaking, insulin seems to affect primarily the part or organ which is in the most active stage of development or differentiation at the time of injection, although the growth of the chick embryo as a whole is retarded to a degree varying with the dose of insulin.

3. Dr. Martin Sonenberg[34] of the Memorial Hospital working with tagged hormones, has very recently found that radioactive labelled pituitary growth hormone shows a marked and significant localization in the pancreas, with lesser concentrations in the liver, the thymus and the kidney. This may have some bearing on the work of Young.

Insulin labelled with radioactive iodine showed surprisingly large amounts localized in the convoluted tubules of the kidney, in amounts equal to the deposits in the liver. What the significance of this will be, requires further study. This research on these labelled hormones is being actively followed.

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THE THERAPEUTIC EVALUATION OF CORTISONE APPLIED TOPICALLY IN OPHTHALMIC DISEASES*

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SINCE Henderson and Hollenhorst,[1] who were probably the first to study the effect of cortisone in ophthalmic disease in October, 1949, numerous articles on this subject have appeared in the literature. More recently the local use of cortisone in the treatment of eye disorders has been reported by various workers.[2 to 11] Because the topical use of cortisone in the eye does not result in any systemic absorption of the drug this mode of administration in the treatment of ocular lesions offers obvious advantages. Especially is this so when the ocular lesion occurs in a patient with tuberculosis, diabetes, vascular hypertension, or a psychosis, all of which conditions contraindicate the parenteral use of cortisone. The topical administration further permits treatment over relatively long periods of time without hospitalization or daily observations of the patient.

At no time has it been demonstrated that any ocular disease is caused by a deficiency of 11-dehydro - 17 - hydroxy - cortico - sterone. Consequently the use of cortisone in the treatment of ocular lesions does not constitute replacement therapy. Rather it is believed that cortisone operates at the tissue level by inhibiting fibroblastic activity and decreasing membrane permeability, that is, decreasing inflammatory or allergic transudation and cell extravasations. It does not however, act through any fundamental inhibition in the antigen-antibody reaction, nor does it act directly upon bacterial or viral organisms causing the inflammation. Hence, cortisone may be strikingly beneficial in the treatment of ocular lesions displaying marked exudative reactions, whether due to foreign proteins or to bacterial allergens as in phlyctenular keratitis and non-granulomatous iritis, but unless the causative factor of the inflammatory disorder has been removed, or time has permitted the natural defence mechanism of the body to develop its own immunity, upon withdrawal of cortisone the original inflammatory reaction may return. Further, where the inflammatory reaction represents a defence mechanism against a direct bacterial or viral invasion, cortisone may actually prove harmful by suppressing the exudative phases of the inflammatory reaction and yet permitting the propagation of the organisms causing the infection. Consequently, cortisone therapy should not become a repository for hopeless cases, nor should its adoption be an excuse for ignoring a diligent search for the cause of the disease and eradicating this whenever possible. In addition, when the precise bacterial organism is known, cortisone treatment should be augmented by appropriate antibiotic therapy.

It has been the object of this study to treat topically 100 cases of various ocular conditions with cortisone using several different preparations to determine: (1) If one form and concentration of the drug is more effective than another. (2) If one anatomical ocular structure is more amenable to cortisone therapy than another. (3) If the duration of the lesion prior to the onset of cortisone therapy is a factor in success or failure of treatment. (4) If the etiology of the lesion, whether inflammatory, traumatic, or degenerative is a consideration in success or failure of treatment.

The preparations used were a 1% suspension of cortisone acetate and succinate in 0.9% sodium chloride and 1.5% benzyl alcohol for a preservative. In addition a 1% and 2.5% acetate ointments in a bleached petrolatum base were employed. The drug was instilled into the conjunctival sac every hour or every two hours during waking hours. In almost every case the drug was well tolerated and produced no ocular discomfort. The longest duration of treatment was three and one-half months and caused no

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deleterious effect upon the conjunctival or corneal epithelium. In six cases minims 1 of 1.2% cortisone succinate was injected subconjunctivally daily for from two to ten days. In three of these cases treatment was augmented by topical applications.

From the data appearing in Table I it cannot be said that one drug possesses any therapeutic advantage over another. Woods,[11] believes the ointment is preferable to the drops because of its ease of administration and its instillation can be less frequent. On the other hand Swan,[12] objects to the use of ointments on the grounds that where a corneal abrasion exists the epithelium may grow over globules of oil and being unstable, may later break down.

The experience gained from the subconjunctival use of cortisone in this study is so limited that no conclusion can be formulated, but McLean,[10] recommends this mode of administration for deeper ocular involvement, that is, posterior segment disease. Rome,[13] states that a single dose maintains its effect for 10 to 14 days. He injects 0.4 to 0.6 c.c. of undiluted cortone "Merck" under the conjunctiva 5 to 6 mm. above the upper limbus after first anæsthetizing the eye with pontocaine and a pledget of 10% cocaine placed at the site of injection. Subsequent injections if indicated are given at different sites.

In nearly all of the cases treated the patient reported prompt and often dramatic relief from ocular discomfort and pain. Consequently, in the evaluation of the results, objective signs such as diminution in ciliary congestion, keratic precipitates, aqueous ray, cells in the anterior chamber, and vitreous opacities were the criteria employed. Controls, which were admittedly difficult to obtain in this study, constituted a comparison of the results achieved by the use of cortisone as compared to the results obtained from standard therapy before cortisone treatment was begun, bilateral cases in which one eye only was treated while the contralateral eye was used as a control, and finally, relapses were noted following the cessation of cortisone therapy.

The results were classified as: (1) "Cured" providing there was minimal coexisting therapy, some measure of control, and an adequate period of observation to exclude a relapse. (2) "Improved" where despite the subsidence of objective signs the response to treatment may have been due to other therapy such as H-antigen typhoid in the management of a case of uveitis, or the period of observation was inadequate to exclude a relapse. (3) "Unimproved". (4) "Worse" where there was an aggravation of symptoms despite the use of cortisone.

In the analysis of the statistical data shown in the tables, for the sake of brevity the number of cases presented as "cured" and "improved" has been grouped together, and similarly cases labelled as "unimproved" and "worse" have been combined. These figures have been presented in percentages of the total.

TABLE I.

DRUG USED

Drug	*No. cases*	*Cured*	*Improved*	*Unimproved*	*Worse*	*Success*	*Failure*
Cortisone acetate suspension 1%.....	69	7	35	26	1	61%	39%
Cortisone succinate suspension 1%....	2		2			100%	
Cortisone acetate ointment 1%.....	3		3			100%	
Cortisone acetate ointment 2.5%.....	16	3	6	7		56%	44%
Combined suspension and ointment....	4	1	1	1	1	50%	50%
Cortisone succinate suspension 1.2% subconjunctival injection.....	6		3	2		67%	33%
Total.....	100	12	50	36	2		

It is to be expected that the lesions affecting the more superficial tissues of the lids and globe would be more responsive to treatment than deeper lesions because of the higher concentration of the drug. This belief is supported by the data in Table II in which there is a higher percentage of successes affecting lesions of the anterior segment of the globe (cornea, iris, ciliary body, and anterior uveal tract), and a far higher percentage of failures of lesions affecting the posterior segment. The two lid lesion failures represent cases of chronic conjunctivitis, one of which cultured *Strep. hæmolyticus* and the other a yeast organism. The single success noted in the posterior-anterior segment group was a case of a corneal ulcer occurring in a leucoma secondary to glaucoma of long standing. The ulcer healed

promptly with cortisone therapy but the fundamental ocular pathology remained unchanged. The anterior segment group included numerous cases of iritis. It is interesting to note that the cornea did not provide a notable barrier to the penetration of cortisone even when the epithelium was intact. But whether a higher concentration of the drug could be obtained intraocularly, and hence a greater percentage of cures, in cases of iritis with a coexisting abrasion of the epithelium, or by administering the drug subconjunctivally, or by iontophoresis, could not be determined from this study.

In Table III it is seen that there is a significantly higher percentage of cures and improved cases among those of recent origin, particularly those of less than one month's duration. This is to be anticipated when one considers the histopathology of these lesions, acute cases being characterized by a maximum degree of exudation, while chronic cases favour cellular infiltration and fibroblastic proliferation. As Wood,[11] aptly states, "Dramatic as is the effect of these agents (ACTH and cortisone) in inflammatory and exudative disease, they cannot be expected to impart new life to dead and degenerated tissue".

Table IV lists the causative agent according to whether it was inflammatory, traumatic, or degenerative, and these have been further subdivided as indicated. Lesions resulting from bacterial allergens, that is, some remote focus of infection, show a greater preponderance of good results than those arising from direct bacterial or viral infections. For instance, as will be seen subsequently in Table V, beneficial results were obtained from the use of cortisone in 4 out of 4 cases of marginal ulcers of the cornea in which condition the lesion results from an exotoxin whose bacterial focus is usually found on the lid margin. In contrast, representing the direct bacterial and viral inflammatory group, are six cases of dendritic keratitis, three of which were improved and three unimproved. Considering that dendritic lesions exhibit a minimal degree of exudation it is to be expected that cortisone, which has no influence upon the virus itself, will be of questionable value in the treatment of such conditions. This clinical observation is confirmed by the experimental work of

TABLE II.

ANATOMICAL STRUCTURE

Anatomical structure	*No. cases*	*Cured*	*Improved*	*Unimproved*	*Worse*	*Success*	*Failure*
Lids	2			2			100%
Lids and anterior segment	4		3	1		75%	25%
Anterior segment	87	11	47	27	2	67%	33%
Posterior segment	1			1			100%
Posterior and anterior segment	6	1		5		17%	83%
Total	100	12	50	36	2		
Anterior segment						66%	34%
Posterior segment						14%	86%

TABLE III.

DURATION BEFORE TREATMENT

Duration	*No. cases*	*Cured*	*Improved*	*Unimproved*	*Worse*	*Success*	*Failure*
Acute +	31	3	19	8	1	71%	29%
Acute ++	22	5	13	4		82%	18%
Acute +++	9	2	6	1		89%	11%
Acute ++++	2		2			100%	
Chronic +	1	1				100%	
Chronic ++	2		1	1		50%	50%
Chronic +++	5		2	3		40%	60%
Chronic ++++	28	1	7	19	1	29%	71%
Total	100	12	50	36	2		

Acute + Up to one week.
++ Up to two weeks.
+++ Up to three weeks.
++++ Up to four weeks.

Chronic + From one to two months.
++ From two to three months.
+++ From three to four months.
++++ Over four months.

Thygeson,[14] in which he concluded that experimental herpes-simplex virus keratitis in the rabbit produced by three strains of virus in a series of seven experiments, failed to respond to cortisone administered intramuscularly, subconjunctivally, or by instillation into the conjunctival sac.

There were two cases (not specifically mentioned) in this series of 100 cases which developed a drug dermatitis while on topical cortisone. One case resulted from scopolamine and a second from atropine. In a third case with a known atropine sensitivity the drug allergy remained controlled so long as cortisone was given simultaneously.

Though the number of burn cases treated in this series is limited, the results are encouraging, so that cortisone by limiting fibroblastic proliferation may prevent both corneal scarring and the formation of symblepharon. The two failures noted among the six burn cases may be attributed to the inadequate dosage of the drug in the presence of the intensity of the inflammatory reaction caused by the severity of the burn.

From an analysis of these data in Table IV it would appear that perhaps the greatest use of topical cortisone lies in the treatment of the postoperative intraocular surgical case in which, as a result of trauma and consequent liberation of histamine, an intense exudative inflammatory reaction ensues. Such a reaction is most marked in extracapsular lens extractions in which the absorption of the lens protein represents an additional insult to the eye. The extracapsular lens extractions reported represent either linear extractions for congenital cataracts, Homer-Smith extractions for complicated immature cataracts, or attempted intracapsular extractions which failed because of intumescence of the lens. Because cortisone is believed to interfere with wound healing it was not used until the seventh postoperative day at which time relatively firm, fibrous union of the corneal section has occurred.

Hogan[15] and Henderson[1] report successful results of intraocular surgery in the presence of cortisone given parenterally. In fact cortisone therapy through its action of retarding fibroblastic tissue formation may increase filtration and so be useful in the early postoperative management of fistulizing operations for glaucoma. In general, however, the use of cortisone in the early treatment of postoperative eye cases must be viewed guardedly. Leopold[7] has shown in rabbits a definite delay in the healing of corneal epithelium following abrasions. This finding was not observed clinically in this series of cases. Cortisone will interfere with the fibroblastic proliferation which occurs early in wound healing, but once this has formed cortisone will not destroy it. Cortisone, then, may strikingly diminish the inflammatory reaction consequent on intraocular surgery but where the success of the operation is dependent upon strength of adhesion as in operative treatment of retinal detachment the use of cortisone may be contraindicated.

Table V lists the types and number of cases treated with local cortisone and may afford some predictive information as to the type of case in which the topical use of cortisone is likely to succeed or fail.

Because the literature fails to report any cases in which cortisone topically applied aggravated the lesion being treated, the two cases which

TABLE IV.

	ETIOLOGY						
Type	*No. cases*	*Cured*	*Improved*	*Unimproved*	*Worse*	*Success*	*Failure*
Inflammatory							
Bacterial and viral—direct	13		6	7		46%	54%
Bacterial allergen	31	2	18	9	2	65%	35%
Allergic	1			1			100%
Chemical acid	3		2	1		67%	33%
Chemical alkali	3		2	1		67%	33%
Trauma							
Direct	14	3	6	5		64%	36%
Postoperative							
Intracap. lens extract	9	4	3	2		78%	22%
Extracap. lens extract	17	3	11	3		83%	17%
Other	1		1			100%	
Degenerative	8		1	7		13%	87%
Total	100	12	50	36	2		

definitely became worse during the administration of cortisone invite comment. Both of these were cases of non-granulomatous iritis accompanying rheumatoid arthritis, in which condition uveitis is a complication in 2 to 5% of cases. The first case was one of chronic iritis with a seclusion of the pupil and complicated cataract. Immediately following the use of 1% cortisone acetate drops the patient complained of ocular discomfort, and increase in the objective signs was noted, and the intraocular tension rose from 25 to 35 mm. of Hg., Schiotz. Cessation of cortisone resulted in the restoration of these findings to pre-therapy level. In this case, previously reported in another paper,[16] the cortisone drops may have caused a local imbibition of fluid embarrassing an already crowded anterior chamber angle and thus precipitated the secondary glaucoma. The second case was one of a mild iritis of recent origin who had had a previous attack in the same eye four years ago. The use of 2.5% cortisone acetate ointment q.2h. resulted in marked discomfort, exacerbation of the iritis, clouding of the vitreous, and a deterioration of vision from 20/20 to hand movements. No improvement resulted by substituting 1% cortisone acetate solution for the ointment. Later the patient admitted a drug sensitivity to atropine, which drug had also been used from the start of treatment. Substituting scopolamine for the atropine and deleting the cortisone resulted in a prompt cessation of the iritis. In both of these cases there was no aggravation of the systemic disease to explain the apparent deleterious effect of the cortisone therapy.

TABLE V.

	DIAGNOSIS							
Diagnosis	*No. cases*	*Cured*	*Improved*	*Unimproved*	*Worse*	*Relapse*	*Success*	*Failure*
Conjunctivitis	2			2				100%
Keratitis dendritic	6		3	3			50%	50%
Keratitis punctata	1		1			1	100%	
Keratitis disciform	2		1	1			50%	50%
Corneal abscess—post traumatic	1		1				100%	
Keratitis?	2		1	1			50%	50%
Cornea marginal ulcer	4	1	3				100%	
Keratitis interstitial luetic	1							100%
Keratitis interstitial tuberculous	2		2				100%	
Keratitis profunda	1		1				100%	
Keratitis phlyctenular	4		4			1	100%	
Corneal ulcer inflammatory	1		1				100%	
Cornea chemical burn alkaline	3		2	1			67%	33%
Cornea chemical burn acid	3		2	1			67%	33%
Cornea ulcer traumatic	5	2	2	1		1	80%	20%
Keratitis traumatic	2	1		1			50%	50%
Keratitis rosacea	1			1				100%
Keratitis bullosa	2			2				100%
Corneal leucoma int. keratitis	1			1				100%
Cornea epithelial dystrophy	1			1				100%
Cornea leucoma post-glaucoma	3		1	2			33%	67%
Iritis non-granulomatous	13		7	4	2	2	54%	46%
Iritis granulomatous	1			1				100%
Iritis traumatic	4	1	3				100%	
Iritis postop. extra. lens ext.	17	3	11	3		1	82%	18%
Iritis postop. intra. lens ext.	9	4	3	2			78%	22%
Iritis postop. diathermy	1		1				100%	
Endophthalmitis	1			1				100%
Sympathetic ophthalmia	1			1				100%
Uveitis post. non-granulomatous	2			2				100%
Uveitis Boeck's sarcoid	1			1				100%
Globe intra-ocular F.B.	1			1				100%
Globe black-ball hæmorrhage	1			1				100%
Total	100	12	50	36	2	6		

SUMMARY AND CONCLUSIONS

One hundred cases of various types of ocular lesions have been treated topically with cortisone. Although valid conclusions derived from statistical data when applied to a clinical problem in which controls are difficult to obtain, are open to both criticism and error, it would appear from an analysis of these data that cortisone administered topically either in the form of drops or ointment is significantly more effective in the treatment of:

1. (a) Structures involving the anterior seg-

ment of the eyeball rather than the posterior segment. (b) Cases of recent onset rather than chronic cases. (c) Ocular lesions due to bacterial allergins, burns, and trauma, less effective in inflammatory lesions due to direct bacterial and viral invasion, and not effective in degenerative conditions.

2. Two per cent of the cases treated became worse while on cortisone applied topically. This result necessitates constant observation of patients on this form of treatment.

Acknowledgment is made to Dr. Marvin Darrich of the Department of Biochemistry at the University of B.C. for initiating this project and furnishing the cortisone used in this study through the courtesy of Merck and Co., Montreal, P.Q.

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OBSERVATIONS ON THE PHYSIOLOGICAL EFFECTS OF CORTISONE AND ACTH*

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IN THE CLINICAL USE of ACTH and cortisone widespread physiological effects of both desirable and undesirable nature may occur. Their incidence and clinical implications are important in considering the use of these hormones in the individual patient. At the Metabolic Unit of the Vancouver General Hospital a group of 27 cases have received cortisone or ACTH for 28 days or longer. A number of disease states are represented including idiopathic steatorrhœa, regional ileitis, ulcerative colitis, nephritis, rheumatoid arthritis, scleroderma and dermatomyositis.

It is the intention of this paper to report the observed effects of these hormones on normal tissues and physiological mechanisms. The results obtained in the treatment of the morbid states will be covered in separate reports.

Method.—All cases were put on a salt-poor diet (no added salt) and given measured quantities of fat, protein, and carbohydrates. Gross fluid balance was estimated (*i.e.*, fluid intake and urinary output). The serum electrolyte pattern was followed in 14 cases, and estimations of plasma cholesterol, blood proteins, fasting blood sugar, hæmoglobin, white blood counts and differential counts were followed in all cases. Blood pressure, weight, and apex rate were observed daily before breakfast. Electrocardiograms and roentgenograms of the chest were done periodically.

The chief physiological effects observed, their incidence and suggested management are noted below. Since the administration of ACTH and cortisone in general appeared to produce similar results, no attempt is made to divide the two groups, except where some definite difference was encountered.

(a) BODY FLUIDS AND ELECTROLYTES

1. *Serum potassium levels.*—Serial observations were made in 14 cases. Estimated serum levels showed variations of up to 2.9 mgm. % in the control periods. Slight falls of from 1 to 3.5 mgm. % below the lowest pre-treatment levels occurred in 8 cases, while serum levels were unaltered or even increased slightly in the remainder during therapy. In no case was there at any time clinical evidence of potassium depletion such as muscular weakness, respiratory embarrassment or cardiac arrhythmia.

It has been the experience elsewhere[2] that an occasional patient has an exaggerated electrolyte response to these hormones. Such a case, on therapeutic levels of cortisone or ACTH, will develop a hypokalæmic, hypochloræmic alkalosis. Cessation of hormone therapy and other therapeutic measures may be necessary.

Management.—As a prophylactic measure or where low potassium in a problem during ther-

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apy, 2 to 6 grams of potassium chloride can be given daily in divided doses as a supplement to the regular diet. Where there is a renal lesion, potassium should be used with caution.

2. *Salt and water retention.*—It has been demonstrated elsewhere that water retention is due to the sodium-retaining effect of the hormone on the renal tubules. Water retention was one of the commonest side effects in this series, being noted in 9 out of 23 cases observed. These 9 cases had clinical evidence of fluid retention with weight gain of 3 to 12 lb. which was lost subsequently by spontaneous or induced diuresis. An additional 9 cases showed a weight gain during treatment that was evidently a true tissue increase as it was not attended by evidence of fluid retention and was maintained after the drug was discontinued. The tendency to retain fluid was aggravated when hormone dosage was increased. It was frequently noted that some individuals who did not retain fluid on doses of 100 mgm. of cortisone daily, promptly did so on doses of about 200 mgm. daily with gain of weight and decrease of urinary output.

Before objective signs of œdema were seen, patients would often complain of fullness in the face or tightness of the skin in legs or arms. Pitting œdema was frequently not demonstrable until after about seven to ten pounds gain in weight, and was usually first seen along the shin margins. Gain in weight of two to three pounds a day could always be taken as evidence of fluid retention rather than true weight gain.

Serum sodium levels showed no significant changes but sodium balance studies were not carried out.

As a rule the water retention was not progressive or sustained. After a fluid retention of only a few pounds, a "spontaneous" diuresis usually occurred (despite continued use of the hormones) in the first or second week. This diuresis has been attributed by others[3] to certain effects on renal tubular, as well as glomerular, function. In the absence of this "spontaneous" effect, a diuresis almost invariably occurred if the dose was lowered, or discontinued. This post-treatment diuresis was often delayed three to seven days with intramuscular cortisone due to the "depot" effect which was not noted with oral cortisone or ACTH.

Management.—Due to the part sodium plays in the retention of fluid a low sodium diet has been advised[4] as a prophylactic measure. The extent of this sodium restriction can be designed to meet the particular clinical situation. With a "salt poor diet" (about 5 to 6 grams of NaCl) 9 of our 23 cases showed clinical evidence of fluid retention. A more rigid sodium restriction might have been more successful in control of fluid retention. When it is desired to carry on with the hormones despite increasing fluid retention, or when retained fluid causes embarrassment, a mercurial diuretic will produce a prompt but unsustained effect (see Fig. 1). In two cases of this series mercurial diuretics were used due to rapid fluid accumulation, but it was also

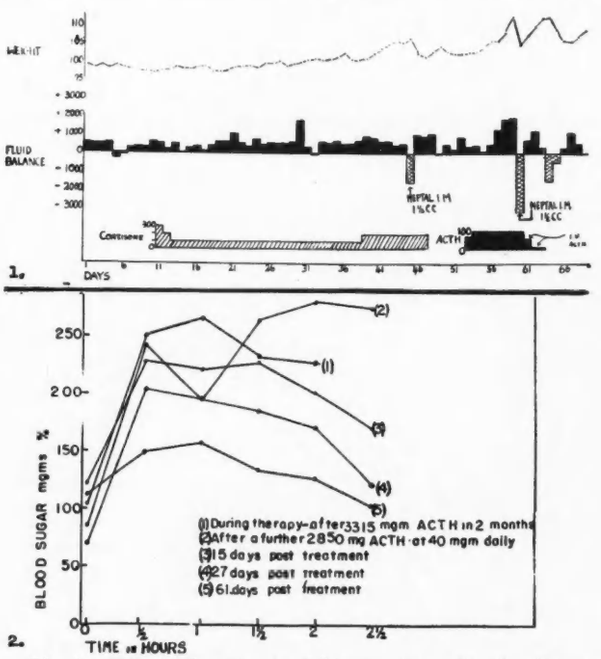


Fig. 1.—Effect of neptal in fluid retention. **Fig. 2.**—Upset in carbohydrate metabolism occurring during ACTH therapy. The impaired sugar tolerance curve has returned to normal by 61 days' post-treatment (9 year old female child).

necessary to reduce or discontinue the dose of hormone. In both cases the fluid rapidly re-accumulated following the induced diuresis, when the dose of hormone was maintained at the same level.

It must be remembered that any substantial diuresis may cause a rapid depletion of body potassium which may be important if there is already depressed serum potassium. In none of our cases did this situation develop, but it may be well to protect the patient by giving additional oral potassium chloride when a diuretic is being used.

Because of frequency of induced fluid retention these hormones should be used with caution in the presence of pre-existing circulatory or renal impairment.

(b) INTERMEDIARY METABOLISM

1. *Carbohydrate metabolism.*—On ACTH therapy one young patient developed transient diabetes which persisted for more than 27 days after discontinuing treatment. Glucose tolerance curves are shown in Fig. 2. No ketosis was apparent at any time and fasting blood sugars were usually normal. Blood sugar tolerance was normal by the 62nd day. This case also presented a marked alteration in fat deposition as described below (Fig. 3).

This carbohydrate metabolic upset which occurs occasionally during therapy differs in several respects from true diabetes mellitus according to Wilder.[5]* Sprague states in a recent review[1] "there have been a few instances in which cortisone or ACTH had rather pronounced diabetic effects". "The majority of patients treated with cortisone or ACTH have not exhibited clinically significant impairment of carbohydrate tolerance." It has been suggested that persons with a diabetic tendency or subclinical diabetes may develop clinical diabetes following the use of these hormones. However, this appears to be uncommon.

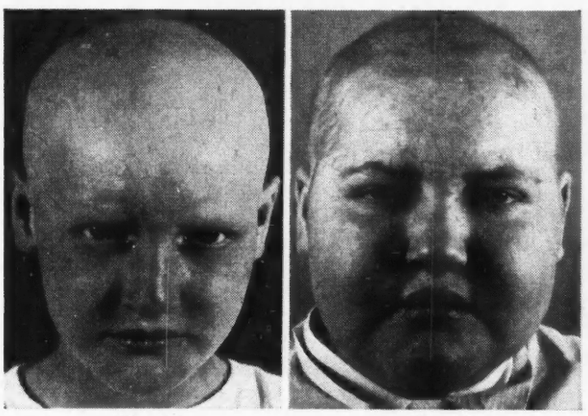


Fig. 3a Fig. 3b

Fig. 3a.—Before therapy. Demonstrates development of marked moon face and acneform lesions (together with hair growth) in patient on prolonged ACTH therapy. Hair fell out after therapy discontinued. Fig. 3b.—After 6 gm. ACTH.

Management.—The majority of reported cases with upset in carbohydrate metabolism have reverted to normal when the hormones have been discontinued as in the case noted above, even though, as in this case, it may take time. Cases of diabetes mellitus requiring adreno-cortical therapy have an increased insulin requirement during therapy[6] and insulin dosage must be adjusted. However, the presence of diabetes is not a contra-indication to the necessary use of these hormones.

2. *Fat metabolism.* — 11 of 27 cases in this series developed a definite moon facies the most marked instance being shown in Fig. 3. This child received prolonged ACTH therapy and also developed the typical fat distribution of a Cushing's syndrome with a cervico-dorsal "buffalo hump"' and fat deposits in the trunk region, (as well as the marked disturbance of carbohydrate metabolism referred to above).

Management.—In all but one of the cases the moon face disappeared spontaneously in a few days after treatment was discontinued. In the case shown in Fig. 3 there has been gradual regression of the abnormal fat distribution and improvement in the body contour, and appearance is normal two months after cessation of therapy (corresponding in time with the recovery from the disturbance in carbohydrate metabolism above). Hench[7] has stated that the concomitant use of œstrogen in small doses may prevent this complication from occurring.

Cholesterol levels were followed in 10 cases and progressive increase in cholesterol levels in the blood were seen in 7 of 10 cases while the hormone was continued. Most marked elevation occurred in two cases of nephritis and in one case of dermatomyositis. In the renal cases the cholesterol rose from 200 to 520 mgm. % and from 320 to 690 mgm. % respectively. Within a few days after treatment was discontinued elevated levels returned to pre-treatment values.

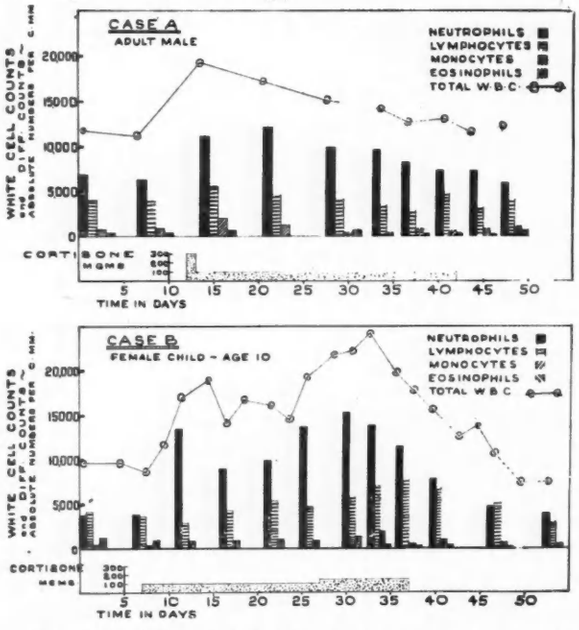
Blood pressure. — Some elevation of blood pressure occurred in 10 of 23 cases but was unsustained after treatment was discontinued except in one case of scleroderma where death from malignant hypertension occurred. In general there was a rise of from 5 to 10 points systolic and diastolic. Excepting the case of scleroderma mentioned the elevated blood pressure responded rapidly to lowering dose or discontinuing the drug. This case will be the subject of a separate report.[8]

Fever.—16 out of 27 cases had some pre-existing elevation in temperature ranging from 99.2 to 100.2° F. In 9 cases the fever subsided rapidly when ACTH or cortisone was started. In 7 cases there was no effect apparent on fever even when dose of the hormone was increased. On the other hand, fever developed in two cases

*According to Wilder:5 (1) It is highly resistant to insulin. (2) It is accompanied by azoturia. (3) It is accompanied by an increase of glycogen in the liver. (4) It responds to fasting much more promptly than does diabetes mellitus. (5) It is usually accompanied by some other evidence of adreno-cortical hyperfunction. (6) It is transitory, the blood sugar levels returning to normal when the adreno-cortical hyperfunction is corrected.

on therapy. One case, a hypertensive subject, developed a chill and fever of 102° following an intravenous heparin injection of 50 mgm. Another patient developed fever and tachycardia with pleurisy.

Pain.—As a general rule pain was relieved whether it was of the bowel, joint, bladder or eye. This usually occurred within 2 to 3 days and was often dramatic. In view of the above effects on pain and temperature these hormones may mask certain clinical manifestations of disease. Cases have been reported where signs and symptoms of visceral perforations were masked during hormone therapy.[9]



Figs. 4a and 4b.—Changes in absolute numbers of white blood cells in adult male and child during cortisone therapy.

Hæmatological changes.—In 18 of 27 cases there was some evidence of bone marrow stimulation with increase in the venous white blood count. The characteristic changes found in the absolute levels of the white cells are shown diagrammatically in Fig. 4. There was usually a marked neutrophil leukocytosis most apparent in the children but also occurring in adults. In children this leukocytosis was usually sustained throughout treatment as shown in Fig. 4b. In the children there was usually an initial lymphopenia which was later followed by an increase in the lymphocytes to initial levels or a lymphocytosis above initial levels. In the adults, in general, the initial leukocytosis was unsustained and significant initial lymphopenia did not occur.

One of the most striking hæmatological effects is the eosinopenia which occurs regularly with the use of ACTH but less commonly with cortisone. In this study eosinophile counts were done regularly in 13 cases during the course of cortisone therapy. In the majority, cortisone produced an initial mild eosinopenia followed by a return to pre-treatment levels despite continuing the hormone. Increasing the dose had either a transitory or no effect on eosinophile levels. However in 5 of the 13 cases there was observed a peculiar effect on eosinophiles which is illustrated in Fig. 5a. Following the initial mild depression the eosinophiles rose to considerably higher levels despite continued treatment with cortisone. This occurred in the 3rd and 4th weeks in all 5 cases. It is possible that in these cases the weak direct eosinopenic effect of the exogenous cortisone has been followed by the suppression of some more potent endogenous eosinopenic agent (corticoid suppression by cortisone?).

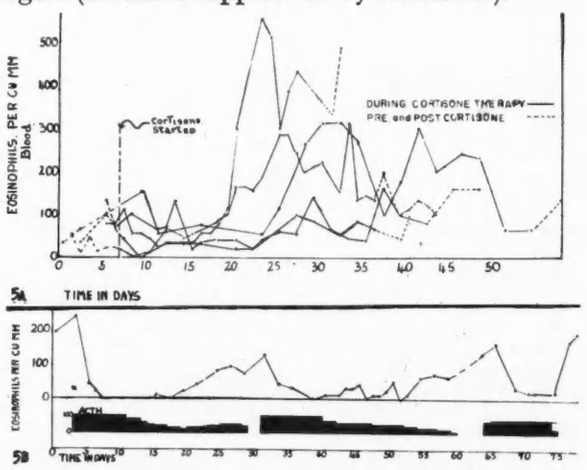


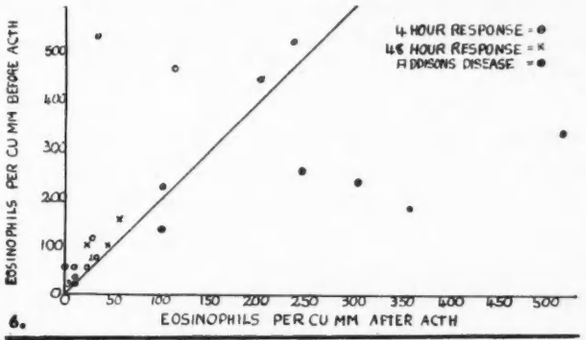
Fig. 5a.—"Escape" of eosinophiles from initial eosinopenic effect of cortisone (intramuscular). **Fig. 5b.**—Eosinopenic effect on ACTH (intramuscular).

The eosinopenic response to ACTH on the other hand was more constant (Fig. 5b). This type of response was consistently noted in this series. Our experience would suggest that the eosinophile counts cannot be used to judge adequacy of the dose where cortisone is used, but are of value in the case of ACTH.

Fig. 6 illustrated the expected eosinophile response to measured doses of ACTH in the test of adrenal cortical function as devised by Thorn *et al.*[10] Of the 19 cases with clinically normal adrenal function 17 showed a fall of over 50% of the circulating eosinophiles. 4 of these were delayed 48 hour responses. The 2 cases with inadequate response were both suffering from acute allergic states. One had acute atopic dermatitis and the other acute asthma. In both instances eosinophiles may have been formed

more rapidly than they were being depressed by the hormone. 2 cases of Addison's disease are also represented, both of which show the expected negative eosinophile response.

Sedimentation rate.—19 cases had an elevated sedimentation rate (Westergren). Of these, 16 showed a marked decrease and 1 a slight decrease in the rate during treatment. In 2 cases with normal initial sedimentation rate there was a rise during therapy which reverted to normal while therapy was still continued. In 2 cases a difference in the response of the sedimentation rate to intramuscular and oral cortisone was apparent. In these cases the sedimentation rate responded quickly to oral cortisone, worsened on intramuscular cortisone, improving again on oral cortisone (Fig. 7). This effect has been noted



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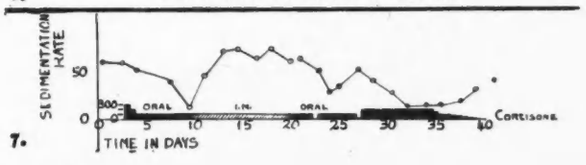

7.

Fig. 6.—ACTH test of adrenal cortical function. Note that all individuals with intact adrenals showed the expected 50% eosinophile drop after 25 mgm. of ACTH except for two individuals with allergic states. Fig. 7.—Paradoxical effect of intramuscular cortisone on sedimentation rate. The sedimentation rate fell initially with oral cortisone rose with intramuscular cortisone only to fall again when oral route was used.

previously by Bagnall,[11] who pointed out that in certain individuals the sedimentation rate may rise with intramuscular cortisone despite improved clinical condition. Such a paradoxical response is not common but must be kept in mind where clinical improvement and sedimentation rate changes are at variance.

Appetite.—Appetite was increased in 22 of 27 cases, in 3 it was unchanged; and in 2 cases it was decreased on treatment. Associated with the increased appetite there was usually some increase in weight which persisted after the drug was discontinued.

Skin.—Acneform lesions which appeared in 2 cases did not present a problem. In one individual small doses of œstrogen effected a rapid improvement in the acne which relapsed when the œstrogen was discontinued. Finally the lesions cleared rapidly on discontinuing hormone therapy. Mild hirsutism occurred occasionally but was not a problem. Excess hair rapidly disappeared when treatment was discontinued. In no case was there any apparent loss of scalp hair. Pigmentation of the skin and nails occurred in one case following prolonged ACTH therapy. Pigmentation was brownish and present in the creases of the palms and in addition there was occasional scattered black and brown pigmented spots on the skin. There was no pigmentation noted in the mucous membranes of the mouth.

Healing. — Retardation of wound healing in hyperadrenal corticism is well recognized and considerable interest in this phenomena has been apparent since Ragan[12] reported interference with wound healing in cortisone treated animals. In several operations performed on patients in this Unit while cortisone or ACTH was being given, interference with healing has not been apparent. These included one case each of arthroplasty of the elbow, arthrodesis of the fingers, cataract extraction, biopsy of the scalp, teeth extraction, and 2 cases of total colectomy. It would appear from these cases that on ordinary therapeutic dosage at least, the problem of interference with healing is negligable.

Mental. — Increased sense of wellbeing with euphoria occurred in 16 of the 27 cases. Mood swings occurred in 6 while 5 remained unaffected. Marked depression or a serious psychosis did not occur in any of this group. Subjective paræsthesias were often present, taking the form of burning pains in the extremities, sharp stabs in the joints or feeling of fullness in the abdomen, face and arms. Sleeplessness was a very common complaint.

Occasionally, in unstable individuals, serious psychosis with elated, depressive or schizophrenic states have been precipitated. This may be persistent and may require special psychiatric measures. Precipitation of such states is apparently uncommon, at least in our experience. Unstable individuals or cases with history of psychiatric disorders present a contraindication to the use of these hormones. The mental effects noted in this series require no discussion. Symptomatic treatment of insomnia and reassurance was all that was required.

Menstrual changes. — Irregularities of men-

strual function were frequent during treatment. Delayed period or lessened flow occurred in many, others showed increase in number of periods. One case of functional menorrhagia which was quite severe was corrected during and following cortisone therapy, and the patient has had normal function since.

Immunological changes. – In one patient a positive tuberculin test was markedly decreased during therapy. Another patient, who exhibited numerous skin sensitivities prior to treatment had a much less marked skin reaction to the same allergens during treatment, with return to pretreatment status shortly after therapy was discontinued.

Depression of adrenal cortex following cortisone therapy.—In the majority of cases there was some evidence of hypocorticism within the week after cortisone therapy was discontinued. There was subjective complaint of loss of wellbeing, depression and easy fatiguability. This was usually only temporary and the sense of wellbeing usually returned after three to four days. The "Thorn" test in all cases revealed a less sensitive cortex with respect to its ability to produce eosinopenia in circulating blood following a dose of 25 mgm. of ACTH intramuscularly. In one individual this depression of eosinophile response was present for 55 days. This is probably the result of an insensitive cortex, rather than a cortex which is unable to respond, for we have been able to produce a rapid and complete fall in the eosinophiles immediately following a six week course of cortisone with larger doses of ACTH given by intravenous drip.

Management.—The use of rest periods of 4 to 6 weeks between courses of treatment is recommended to allow the adrenal cortex to return to its original status. Some clinicians have suggested that cortisone and ACTH courses be used alternatively to prevent atrophy of the adrenal cortex from prolonged course of cortisone alone. Since both drugs apparently depress pituitary ACTH formation this method of prevention may not be entirely satisfactory.

SUMMARY

This report comprises an analysis of the physiological effects observed under controlled conditions in 27 patients receiving ACTH or cortisone therapy for 28 days or longer. Observations were made on fluid exchange, blood electrolytes, some aspects of carbohydrate and fat metabolism, blood pressure, body temperature, peripheral blood counts, erythrocyte sedimentation rate, subjective symptoms, skin changes, and effects on wound healing.

Water retention was the common undesirable side effect of these hormones. It could be controlled in part by salt restriction. In two cases it was necessary to use mercurial diuretics as well, which produced temporary relief, but it was also necessary to discontinue the hormones soon after.

An important disturbance of carbohydrate metabolism occurred in only one case, a child under prolonged ACTH therapy. This patient also developed the most prominent disorder of fat deposition. Evidence of both disturbances subsided within two months.

Interference with wound healing was not observed on the ordinary therapeutic dosage of hormones.

A paradoxical response of the sedimentation rate to intramuscular cortisone was noted in certain individuals. An unexplained increase in circulating eosinophiles occurring after the third week of cortisone was noted in some instances.

Increase in serum cholesterol was observed in three individuals during therapy.

Blood pressure effects were usually minimal or unsustained. One fatality occurred when a case of scleroderma on ACTH developed intractable malignant hypertension.

Although fever was usually reduced, it developed in two cases while on therapy.

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Thanks are due our colleagues in the Metabolic Unit who have allowed us free access to all case material, and especially to Dr. John Eden who was responsible for laboratory arrangements.

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FURTHER EXPERIENCES WITH PARA-AMINOSALICYLIC ACID*

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THIS PAPER is a further communication on our experiences with the concomitant use of oral para-aminosalicylic acid and intramuscular streptomycin in the treatment of pulmonary tuberculosis, as considered from the laboratory aspect.

Since our last report[1] was published, the use of combined therapy of this nature has become a standard practice. It is possible now to come to some fairly well established conclusions:

It is known that the daily oral administration of 12 grams of para-aminosalicylic acid or its equivalent in the form of its sodium salt along with the streptomycin course will definitely delay the development of streptomycin resistant strains of tubercle bacilli as demonstrated by *in vitro* studies of the organisms isolated from the patient. Numerous studies including our own have shown this. Karlson *et al.*[2] in one of the earliest reports of this nature suggested the use of more than one chemotherapeutic agent at once to delay the emergence of streptomycin resistant strains of tubercle bacilli. Subsequent papers have indicated that the best combination is still P.A.S. and streptomycin. Dye[3] has recently suggested the use of three or more chemotherapeutic agents at once in an attempt to further delay the emergence of streptomycin resistant strains. In the same paper he mentions other means of achieving this object, *viz.*: allowing longer intervals between injections of the agent or alternating short courses of different agents.

It is surprising that the clinical significance of a laboratory report that the organisms isolated are "resistant" to streptomycin is still not absolutely settled. Obviously, if all the tubercle bacilli with which the patient is infected be resistant to streptomycin in the concentration to which that antibiotic can be raised in the body, a further course of the drug can have no additional therapeutic value. The question as to whether the organisms isolated from the sputum or gastric washings are characteristic of the complete bacterial flora of the patient or not is still debated. Two papers reported in the Tenth Conference on the Chemotherapy of Tuberculosis of the Veterans' Administration of the United States last January take these opposing views,[4, 5] Armstrong and Walker[6] reported different sensitivities for organisms isolated in different portions of the lung in a post mortem examination of a "resistant" case.

With the use of solid medium it is possible frequently to see a relative change in the morphology of the colonies of *M. tuberculosis* on the plates containing no streptomycin, compared with those with increasing amounts of the antibiotic. Often the resistant strain evident in the latter plates on which the report of "streptomycin resistant" is based may represent only a very small fraction of the flora as shown on the control plate. It is probable that such cases may respond favourably to an additional course of streptomycin despite the laboratory report. In other cases the sensitivity tests show a uniform bacterial growth in all the plates and no evidence of a sensitive strain. It has become customary in this hospital in the event of a contemplated new course of streptomycin despite a previous laboratory report of some degree of resistance, for the clinician to request an appraisal as to the possible value of such a course. In such cases the plates are carefully studied for the existence of sensitive strains which might be eliminated and a report given with this in mind.

Our experience with the concomitant use of streptomycin and P.A.S. began in March of 1948. We have used P.A.S. in various forms. Our dosage has been standardized on the basis of free acid. Consequently a dosage equivalent to 10 gm. of the free acid is achieved by the administration of 13.8 gm. of the dihydrate sodium salt. In the previous report from this hospital[1] was included the laboratory findings in cases treated with 10 gm. P.A.S. and 1 gm. streptomycin daily. Our present study includes many of these cases as well as additional ones.

In December of 1949 it was decided to test the possibility of smaller dosages of P.A.S. in achieving the same effect as the larger. *In vitro* studies[7] had shown that a moderately inhibiting concentration of either drug was markedly enhanced in its effect by a completely non-inhibitory dosage of the other drug. Alternate cases to be put on a course of streptomycin were given in addition either 2 or 10 gm. daily of P.A.S. This method of randomization was carried on for a year when no further cases were

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put on the 2 gm. dosage but the number on course at that time continued to the end.

The bacteriological studies carried on with these patients was similar to those previously reported.[6, 8] Organisms were isolated, where possible, prior to, and at monthly intervals during, and for six months following, the conclusion of streptomycin therapy. The tubercle bacilli were grown on Lowenstein slopes. Subsequently a saline suspension of the bacteria was made and streptomycin sensitivity tests were done by inoculation of a series of Petri dishes containing various concentrations of streptomycin in Herrold's egg yolk medium.[8, 9] The concentrations ranged from a control through 0.5, 2, 5, 10, 25 to 50 micrograms of streptomycin per c.c. Only when the growth on the 50 microgram plate after four weeks' incubation was equal to that on the control was the organism said to be "completely resistant" to streptomycin. Organisms in which an intermediate degree of growth ranging from a one plus growth on the 10 microgram plate to that showing up to three plus growth on the 50 microgram plate were all said to be "moderately resistant". Organisms on which no growth was seen on the 10 microgram or higher plates were said to be "sensitive". These definitions are arbitrary and are the same as those previously used.[1, 8, 11] Because of the possible different clinical significance between "Moderately resistant" and "Completely resistant" strains with the risk of causing confusion these are recorded separately on the tables. However, since their total value is used throughout this paper for the incidence of resistant strains, this number is shown as well.

Streptomycin sensitivity records of the organisms isolated from various cases treated with 1 gram of streptomycin intramuscularly alone were studied. Courses in which satisfactory pre-streptomycin sensitivity tests, during, and post studies were obtained, have been tabulated as to the length of course of streptomycin received (Table I). It is seen that in the group receiving 55 to 99 days of treatment about 2/3 of the organisms which could be isolated after treatment showed some degree of resistance to streptomycin. This group is used as a control for the groups receiving in addition oral P.A.S. 2 gm. or 10 gm. daily. These courses were chosen to be within the same range of length of streptomycin dosage.

Table II shows the results of our studies as to total number of cases with some important percentages indicated. Generally this paper is concerned with two main percentages; the first is the conversion rate which is determined as the number of cases converted expressed as per-

TABLE I.

Bacterial Status of 353 Cases After Receiving Streptomycin 1 gm. Daily

Length of course	*<35 days*	*35-54 days*	*55-59 days*	*>90 days*
Converted	*Rate 17=50%*	*Rate 23=45.8%*	*Rate 67=30.2%*	*Rate 6=15%*
Sensitive	12	19	51	4
Mod. resistant	4	13	58	11
	30% of	45% of	67% of	90% of
Resistant	1 / 17	3 / 35	45 / 154	19 / 34
Totals	34	58	221	40

TABLE II.

Bacillary Status After Various Regimens

Bacillary status	*SM. 1 GM. alone*			*SM. 1 GM. + 2 P.A.S.*			*SM. 1 GM. + 10 P.A.S*		
Converted	67	% 30.3	% of 154	28	% 49.2	% of 30	74	% 50.6	% of 72
Sensitive	51	23.1	33.0	11	19.0	36.6	59	40.5	82.0
Mod. resistant	58	26.2	37.7	11	19.0	36.6	8	5.5	11.1
Resistant	45	20.4	29.3	8	13.8	26.8	5	3.4	6.9
			67%			64%			18%
Total	221	100%	100%	58	100%	100%	146	100%	100%

centage of the total number treated. The second is the incidence of resistance which is determined by the total number of cases with organisms showing increased resistance to streptomycin expressed as a percentage only, of those cases from which organisms were still isolated after completion of the course. This is the reason for the two columns of percentage in the tables. Finally, for purposes of statistical analysis the data has been subjected to the chi-square test[12] and from published tables the probability determined of those differences occurring by chance alone. Differences fairly evident from the percentages are re-emphasized. Naturally studies of this nature assume that the groups being compared are of otherwise identical constitution, and this factor must be considered before definite conclusions can be made.

It is seen that the two courses of P.A.S. have a marked difference in the incidence of organisms showing some degree of resistance. The effect of the 2 gm. dosage does not appear to differ significantly (chi-square equals 0.0138. Probability is more than 4:5) in that respect from that of no P.A.S. The 10 gm. dosage is seen to maintain the effect previously reported in delaying the development of resistant strains, and shows a significantly (chi-square equals 46.81. Probability is less than 1:1,000) decreased incidence of resistant organisms.

The question of conversion rates is difficult to assess in a purely laboratory study such as this, since there is no indication as to what other therapeutic measures are contributing. It is seen that there is a significant (chi-square equals 6.6. Probability is less than 1:100) difference between even the 2 gm. P.A.S. dosage and the control. This is even more definite with the 10 gm. dosage (chi-square equals 18.4. Probability is less than 1:1,000). It is seen that the probability of this difference occurring by chance alone in groups of this size is less than 1 in 100 for the 2 gram group and less than 1 in 1,000 for the 10 gram group. One might conjecture that this difference may be due to an additional effect of the P.A.S. However, it would be surprising if the blood levels of P.A.S. reached by the 2 gm. dosage, though failing to affect the acquisition of resistance of strains of tubercle bacilli when persisting, did cause a decrease in their frequency. The fact that the two dosages of P.A.S. have the same conversion rate in the series studied might also suggest that the control is not well randomized with the P.A.S. courses, but that the two P.A.S. courses are of more similar constitution. In such a case the difference in the two dosages in their effect on delaying the emergence of resistant strains is still evident by comparing one with the other.

The question of whether to include in the cases reported as sensitive those also converted has been disputed. Our findings agree with that of Hughes *et al.*[10] who state that never in their experience have resistant tubercle bacilli been recovered from patients whose sputum has subsequently become positive after 60 or more days of negativity. They felt that the true incidence of bacterial resistance is better expressed as a proportion to the total number of cases treated rather than as a proportion to the number remaining positive at the end of treatment. However this method of recording would add the complicating factor of conversion rate and consequently we have adhered to the usual practice in reporting only the proportion of the cases remaining positive.

SUMMARY

1. A laboratory study of 221 cases receiving between 60 to 90 days of streptomycin 1 gram daily showed 67% of the 154 cases in which organisms persisted after cessation of therapy had organisms which were increasingly resistant to streptomycin.

2. In a second group of 58 cases between 60 to 90 days of streptomycin 1 gm. daily and in addition 2 gm. of P.A.S. daily, 64% of the 30 cases in which organisms persisted after cessation of therapy had organisms with increased degree of streptomycin resistance.

3. In a third group of 146 cases receiving between 60 and 90 days of streptomycin 1 gm. daily and in addition 10 gm. of P.A.S. daily, 18% of the 72 cases in which organisms persisted after cessation of therapy had organisms with increased degree of streptomycin resistance.

4. It would seem that a daily dose of 10 gm. of P.A.S. but not 2 gm., along with the streptomycin course of 1 gm. per day, caused a marked reduction in the number of streptomycin resistant strains of tubercle bacilli isolated after therapy was completed.

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MANAGEMENT OF ERYTHROBLASTOSIS FETALIS*

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ERYTHROBLASTOSIS FETALIS is a hæmolytic disease of the fetus and newborn period which results from iso-immunization in the mother to the type of blood that is present in the fetus. Many methods of treatment have been employed. One of the present popular methods is the use of the replacement transfusion. Replacement transfusion originally named "exsanguination transfusion" was devised by the late Dr. Ross Robertson at this hospital. The first patient with erythroblastosis fetalis to be treated by this method was done in 1925 by Dr. A. P. Hart at this hospital. It was successfully carried out with cure resulting, whereas other members of the same family had died or were helpless mental defectives following kernicterus.

Etiological facts.—95% or more of cases have Rh negative mother who is auto-immunized to Rh positive fetus. The remaining cases are due to iso-immunization to unusual antigens. Rh negative individuals occur approximately in 15% of the white population, 4% of coloured and 0.4% of the oriental races. Rh auto-immunization is very rare in pure coloured races and practically non-existent in the Oriental people. With 15% Rh negative and 85% Rh positive, a family set up with Rh positive husband and Rh negative wife occurs in 1 in 13 marriages. The incidence of erythroblastosis is much less than this. In a large series followed at the Hospital for Sick Children, only about 5% of the pregnant child-bearing Rh negative woman married to Rh positive husbands developed antibodies. Thus, the likelihood of an Rh negative female developing antibodies is only 1 in 20.

METHODS OF IMMUNIZATION

(a) Transfusion—with the large use of transfusion in the past before Rh incompatibility was recognized—a large number of Rh negative females must have received Rh positive blood. There are a few of them returning with erythroblastotic infants, but the majority have apparently not been affected.

(b) Injections of blood for purposes of producing immune serum. It has been found that this is a most disappointing procedure, except where it has been used to increase the potency of serum in a previously immunized person.

(c) Passages of small amounts of blood across the placenta from the fetus to the mother during pregnancy. This is the most frequent method of immunization.

There are 4 main types of erythroblastosis, intra-uterine death of fetus, congenital hydrops, icterus gravis group, and anæmia of newborn.

Intra-uterine death of fetus with maceration may be due to other causes but is frequently found associated with Rh iso-immunization in the mother. Pathological examination of the fetus reveals the changes seen in erythroblastosis.

Congenital hydrops is the condition where the baby is born with generalized œdema and ascites. It is often associated with hydramnios and enlargement of the placenta. The baby is usually pale and may show jaundice. The baby is born dead or survives only a short time.

Icterus gravis is the group which comprises the largest proportion of cases. The clinical manifestations are:—jaundice of varying degrees which commences at or shortly after birth, and may progress to a very marked degree, hæmolytic anæmia which progresses, increased number of erythroblasts in the circulating blood in the majority of cases, enlargement of the liver

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and spleen, hæmorrhagic tendency occasionally with purpura, and kernicterus in certain cases manifested by drowsiness, with or without convulsions, later ending in death or cerebral damage.

It usually occurs in the second or later pregnancy, rarely in the first unless the mother has received a transfusion prior to the pregnancy. The diagnosis is made by the history, physical examination, blood examination of the baby and laboratory studies on the mother's and baby's blood. These studies consist in Rh typing of mother and baby, and testing the mother's blood serum for iso-immunization to the Rh factor and testing the baby's red blood cells to determine whether antibodies are attached to these cells. This will be discussed in more detail later.

Anæmia of the newborn is a type of Rh incompatibility and most of the babies born with anæmia fall into this category.

The following laboratory tests are necessary in the management of erythroblastosis fetalis:— Rh testing, antibody testing, classifying into special Rh groups: heterozygos or homozygos, and Coomb's test on baby's blood. As in all laboratory work, practice and experience are of great value in this procedure. The more definite positive tests are easily recognized, but some bloods are weakly antigenic and it is with these that the mistakes are made.

In the slide test, a heavy suspension in serum (not in saline) of cells to be tested are mixed with a drop of the test serum, then agitated for two minutes and the presence of agglutination noted. If the cells agglutinate then the person is Rh positive.

In the water-bath test, a 2% suspension of cells is mixed with a dilution of the serum, incubated in a water bath for one hour. Then the tube is shaken up and the presence of agglutination noted. At the laboratory at the Hospital for Sick Children both methods are used, one as a check on the other. The errors that come in these tests are from inexperience or the use of weak antibody serum in certain border line cases. There is much more likelihood of calling Rh negative someone who is Rh positive. This is not so dangerous in a recipient because if a person is called Rh negative by mistake, usually further tests are done and the error is picked up. Also, the use of Rh negative blood for transfusion into a Rh positive person causes no damage. If by error an Rh positive donor is called Rh negative and used, it may bring about immunization or a serious reaction in an immunized recipient.

Antibody testing must be done in any Rh negative woman who is pregnant; it is necessary to determine whether she has been immunized to Rh positive cells or not. The antibody test is done in two ways on the serum. A heavy suspension of known Rh positive cells is mixed with the woman's serum by tilting back and forth on a slide and observed for agglutination. Known different group of Rh cells must be used to rule out all types, but as a general rule using CDE will take care of 95% of the tests. To get the actual titre of the immunization, a 2% suspension of the cells is incubated at 37° C. in a water bath with dilution of the serum. It has been found that when the serum is diluted with normal saline the antibodies are shown in about 25%. In the others it is necessary to dilute the serum with albumin and to do this a 20% solution of bovine albumin is used. This is the origin of the term "blocking antibody" referring to the fact that the antibody does not show up if the serum is diluted with saline. When a report from the laboratory reads "1:8 blocking antibodies", it means that the serum has been diluted with albumin. The clinical significance of blocking versus saline antibodies is questionable, but it is found that there are more cases of the blocking type and the deleterious effect on the fetus is probably greater.

Originally bloods were classified as Rh positive (Rh) and Rh negative (rh). Later it was found that there were 8 sub-groups. The terminology which became applied to the genes making up the cell and which is accepted by most is: CDE for Rh positive and cde for Rh negative genes. Each cell has these 3 factors in one or another form *e.g.*, the cells may be CDe, Cde, CdE, cDE, cDe, CDE, cdE, cde. The last one, cde, is Rh negative, the others are Rh positive.

In testing for Rh, there are 2 methods which are used: a rapid slide test, and a test where the cells are incubated in a test tube which is a more accurate test.

Classifying into special Rh group has to be done by a special laboratory technique. With special known sera groups, it is possible to classify the cells into the various Rh sub-groups. In addition to this it is possible to a large degree to tell whether a person is homozygous or heterozygous. This refers to the type of genes that have been obtained from the two parents. If Rh positive genes come from one parent and Rh

negative from the other, then the person is Rh positive heterozygous. If Rh positive from both then the person is Rh positive homozygous. If Rh negative genes from both parents then the person is Rh negative.

It is also possible with known cells to classify the immune serum into the sub-group to which it is immunized.

Coomb's test on the baby's blood determines if antibodies are attached to the baby's cells. This is done by testing to see if any human globulin has been adsorbed to the cell. The baby's cells are washed three times with normal saline, then reconstituted to a 2% suspension. Place two drops of these washed cells and two drops of anti-human rabbit serum in a small test tube. This is read in ten minutes and again after slow centrifugation. The suspension is usually incubated in a water bath before centrifugation.

In doing this test everything must be clean and when the cells are re-suspended after centrifugation, they must be mixed using a clean stirring rod or applicator. If one inverts the tube with the thumb over the end it spoils the test. The errors in this test are due to unfamiliarity with the technique and an out-dated or weak testing anti-human serum. This is also a test that should be reserved for laboratories with special technical facilities.

These laboratory tests should be applied as follows: all pregnant women should be Rh classified. If Rh negative then test for antibodies at monthly intervals, after fourth month of pregnancy. The husband should be classified, if Rh positive, as to Rh group and whether heterozygous or homozygous. If an Rh negative woman who has Rh antibodies in the blood is delivered, cord blood from baby should be taken immediately at birth and tested for antibodies (Coomb's test). If this is positive, then the baby has erythroblastosis and measures must be instituted for treatment.

Treatment of the case depends on the clinical type seen. Macerated fetus requires no treatment. Treatment in the congenital hydrops type is usually of no avail but should be carried out vigorously as in the icterus gravis type, which will be described in detail. The congenital anæmia group require transfusions of blood at intervals until the normal blood production returns.

In treating the icterus gravis type or the common type, there are two methods of treatment—the conservative symptomatic transfusion and the radical replacement transfusion. Both of these have supporters and we will show, as far as possible, the advantages of each.

For transfusion by either method Rh negative blood is used because it is felt that Rh positive blood would be attacked by the antibodies in the baby, and do more damage from agglutination of cells blocking small capillaries and the excess pigment formed causing trouble. This is generally accepted as the correct type of blood to use.

Certain observers believe that using certain criteria one can determine which cases are going to be severe and which are not. In our experience this is true to a point; there are certain cases which are obviously severe from the first, but there are also some cases which for the first 4 or 5 days showed no indication that the process was anything but mild. Later they became very severely anæmic, icteric, kernicteric and died.

In the conservative type of treatment, the patient is transfused as often as the hæmoglobin is found below a certain level. Rh negative blood is used. With this form of treatment at this Hospital, the mortality rate was 16% for 74 cases from July, 1948, to December, 1950.

In replacement transfusion the blood is withdrawn from a large pool of blood usually by passing a cannula in through the umbilical vein to the inferior vena cava. In some clinics it is replaced by the same route, but in others the new blood is put in by another vein, such as the internal saphenous. Rh negative blood is used. By using 500 to 700 c.c. of blood, withdrawing and replacing 20 c.c. at a time, the baby's blood can be replaced up to from 75 to 90% with new blood. This procedure is not without danger and fatal accidents have happened. If the procedure is carried out too rapidly, it may embarrass the baby's heart. If the new blood is allowed to cool off it may shock the baby. Also using too much citrated blood may lower the baby's calcium and produce tetany. These are some of the difficulties that may be encountered. This procedure should not be attempted by anyone who has not had some experience. When replacement transfusion is used calcium gluconate should be injected at the end of the procedure to ensure a normal calcium level in the blood.

The rationale of replacement transfusion is to remove antibodies from the baby and put in blood which will not be attacked by the antibodies. If this procedure is to be carried out, it should be done early, otherwise the benefit is lost. It has been our policy to use it only in cases where the baby is seen under 12 hours of birth. Using this method of treatment, the mortality has been 17% for 105 cases from July,

1948, to December, 1950. This is approximately the same as the conservative type of treatment. We are not convinced entirely, as yet, that this procedure is not without merit.

Diamond and Anderson[1] reported that the use of female Rh negative blood reduced the mortality to a very low figure. We have been unable, in the small number so far tried, to confirm this and so far our figures show no difference whether female or male Rh negative blood is used. In 46 replacement transfusions, there were 8 deaths or a mortality rate of 17%; with 15 conservatively treated, there were 3 deaths or a mortality of 20%.

Following the initial emergency treatment, either conservative or replacement, the hæmoglobin should be followed and the baby transfused when necessary. These repeat transfusions may be necessary up to 5 months of age.

Feeding of the erythroblastotic baby sometimes presents a problem. There is no reason why a mother should not nurse her baby even though the breast milk may contain antibodies. There is so little absorbed that these antibodies have no effect on the baby. Many of these babies develop diarrhœa so that protein milk is the safest artificial food to use.

Premature delivery of the baby, often by Cæsarean section, has been advocated to remove the baby from the mother and avoid the absorption of antibodies. This procedure is without benefit for this purpose and, in addition, it adds the hazard of prematurity and should not be used. In the follow-up after an erythroblastotic baby, mothers with antibodies should be urged to donate blood for use in laboratories. This is the only good source of Rh testing serum.

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AN INVESTIGATION OF HISTAMINOLYTIC ACTIVITY OF SERUM IN PREGNANCY*

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FOLLOWING the description by Best (1929), of a thermolabile substance in lung, kidney and liver, which had a histamine inactivating property, and the unequal distribution of histaminase in the body as further reported by Best and McHenry (1930, 1931), numerous investigations on histaminase have been carried out. Extracts of intestine, kidney and lungs had a powerful histaminolytic action, while those of muscle, blood and other organs showed little or no such activity.

In contradiction, Marcou (1938, 1939), using Barsoum and Gaddum's method (1935), claimed that normal blood, plasma, and serum rapidly inactivate considerable amounts of histamine. This was ascribed to some histaminase being normally present in circulating blood. The histaminolytic power of blood is expressed by Marcou by an arbitrary histaminolytic index "HI", which represents the percentage of histamine destroyed in 30 min. at 37° C. by blood to which 3 micrograms of histamine diphosphate had been added per c.c. Thus he found the HI of normal human blood to be 30 to 50%. In addition, he found the HI decreased in allergic states, and increased in febrile states and in women in labour.

More recently, extensive tests of histaminolytic activity have been carried out by Ahlmark (1944), and Anrep, Barsoum, and Ibrahim (1947), with special reference to pregnancy, and the former critically reviews the literature on the subject. Both used a method in which the inactivation of histamine incubated with plasma or serum is measured biologically.

Using a method similar to that of Marcou, as well as a short simplified method, Anrep *et al.*, were unable to demonstrate histaminolysis in over 150 attempts in normal human plasma or serum; nor in tuberculosis, cancer, allergic states, congestive heart failure or various febrile states could any such activity be found. No histaminolysis was found in the blood and serum of the dog, cat, rat or horse, but doubtful histaminolysis, *i.e.*, HI 5 to 10%, was found in the guinea-pig, goat, and water buffalo, and an HI ranging from 15 to 30%, was obtained in the serum of the pig, camel, sheep and rabbit. In dogs and man, repeated increasing injections of histamine, failed to show any histaminolysis in the serum.

In all, 231 determinations of the HI, were

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Clinical material was obtained for this study from the Department of Obstetrics and Gynæcology, Toronto General Hospital, Toronto, Ontario.

made in 136 cases of normal human pregnancy. They found:

1. A strong histaminolytic agent which appeared in the blood of women during pregnancy. This appeared from the third month of pregnancy and increased throughout the gestation period reaching a maximum toward term.
2. This agent was found only in the plasma or serum, none was present in the red cells.
3. After delivery, the HI of maternal blood begins to fall rapidly, beginning 8 to 9 hours post-partum, so that at the end of 24 hours, it is about one-half, and in 48 hours, to less than one-quarter of its previous maximum. In most cases it had disappeared by the third day, but in several, some activity was present till the fifth postpartum day.

histaminolytic action in the blood of men and non-pregnant women. To determine this slight activity, incubation of the plasma required 22 hours. On prolonged incubation, Anrep found a similar activity, but did not feel that it was due to histaminase, since it was not abolished by inactivation of the serum. Ahlmark found that maximal histaminolysis was reached between the 6th and the 7th month, after which it declined to rise again at term. In addition, he found a rise of from 0 to 58% within 2-3 hours after parturition, whereas Anrep found the HI a few

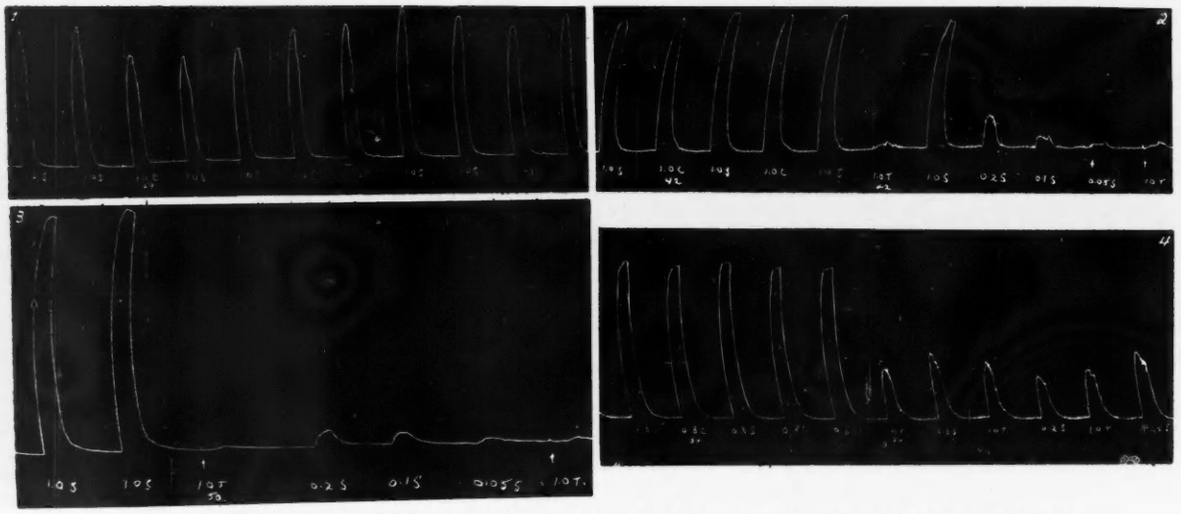

Fig. 1.—This tracing shows how following equal heights of contraction of the preparation to similar doses (1 c.c.) of the standard solution (0.5 x 10-6), that the control is then compared with standard. There is an initial decrease in sensitivity of the preparation with the addition of the serum, but this is soon regained. **Fig. 2.**—No. 42, E.G., age 25. Para I Gr. III. Pregnancy of 29 weeks with HI = 95. 1.0 c.c. of the test contained the same amount of histamine as 0.05 c.c. of the standard solution of histamine diphosphate. **Fig. 3.**—No. 50, Z.E., age 16. Para I Gr. II. 40 weeks, first stage labour HI = 100. No response is seen to 1.0 c.c. of the test solution, although 0.05 c.c. of the standard histamine solution produced a response. **Fig. 4.**—No. 54, R.S., age 38. Para II Gr. III. Pregnancy of 24 weeks HI = 80. Allowing for slight changes in sensitivity of the preparation. 1 c.c. of the test solution most closely approximated 0.2 c.c. of the standard.

4. The human placenta was the source of the histaminolytic agent in maternal blood. The histaminolytic power of the placenta per gram of tissue was 10 to 15 times stronger than that of serum at term. Per gram of tissue, placentæ of different age and weight did not differ greatly in regard to their power to inactivate histamine.
5. No change of histaminolytic power of the blood could be detected in animals in pregnancy and extracts of their placentæ, with the exception of that of the rat, had no power to inactivate histamine.

Ahlmark states that most of the biological, gasometric and colorimetric methods used for the diamine oxidase reaction of blood were insufficiently controlled and made under extremely varied conditions, thus the results were frequently contradictory. All observers agree, however, that the blood of pregnant women shows a conspicuous increase of histaminolysis.

In comparing Ahlmark's and the results of Anrep and others, the former found a weak

hours before and after delivery to be the same.

The rôle of histaminase in the blood during pregnancy is not as yet recognized. Anrep suggests that while it is tempting to ascribe to it a function of histamine detoxification such a speculation is premature. Histaminase is not, however, a specific enzyme and therefore it is quite possible that it has to be considered in connection with some substances other than histamine.

In toxæmia of pregnancy, Ahlmark found values of histaminolytic power of sera deviating from the normal in some cases and there appeared to be no correlation between the degree of symptoms and the histaminolytic power. The results of Kapeller-Adler (1944) are not in agreement. She believes that histamine may be formed in the metabolism of pregnant women from

histidine, present in large amounts throughout gestation, by histidine decarboxylase. In normal pregnancy, most of the histamine is presumably destroyed by histaminase. In mild pre-eclampsia the activity is very low and the histamine formed in considerable quantities exerts its toxic effect, particularly on the kidneys.

Anrep points out that a comparison between the histaminolytic index and other auxiliary manifestations of pregnancy such as the production and excretion of œstrogenic and gonadotrophic hormones is of interest.

There is a similarity between the HI of pregnancy and the A-Z reaction, in that no usual laboratory animal, except possibly the mare gives the A-Z reaction, and none of these show a detectable increase in the HI in pregnancy. On the other hand, the curve of excretion of the chorionic gonadotropin is unlike the increase in HI. The former reaches a maximum on the 50th to 60th day of pregnancy, then falls during the next 20 days to a much lower level, which is then maintained for the rest of the pregnancy. The HI, however, increases to term. The A-Z remains positive from 5 to 7 days, following a full term delivery, whereas the histaminolytic activity disappears more rapidly, usually within 48 hours.

The histaminolytic index follows a curve similar to that of the excretion of the œstrogenic principles during pregnancy. Both appear approximately in the 3rd month, both reach a maximum toward the end of pregnancy, both fall rapidly to very low levels within about 48 hours after labour.

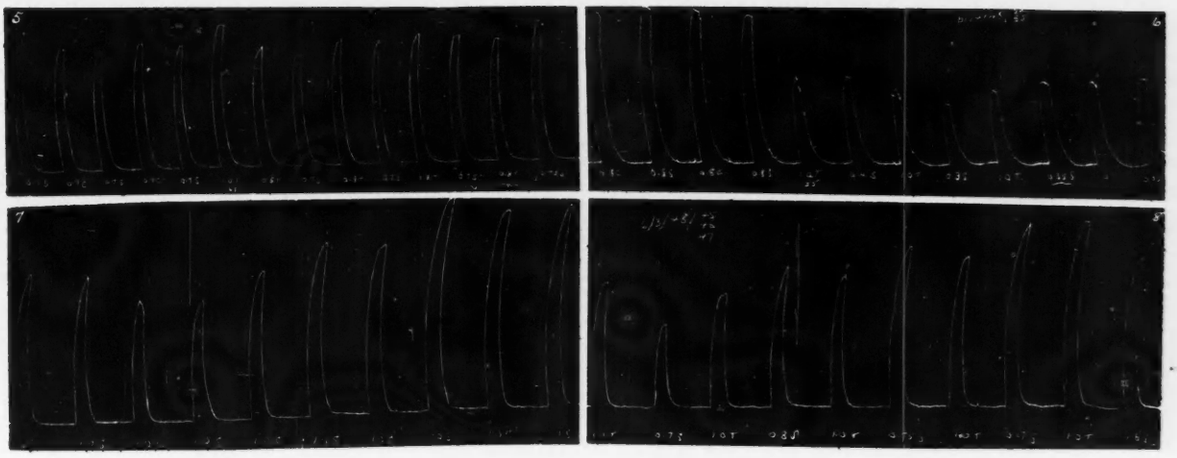

Fig. 5.—No. 65, age 24. Para I Gr. III. Pregnancy of 13 weeks. HI = 15. 0.8 c.c. of the test solution showed the same result as 0.7 c.c. of the standard. **Fig. 6.**—No. 55. J.M., age 21. Para I Gr. II. Pregnancy of 27 weeks. HI = 65. 1 c.c. of the test solution showed the same response as 0.35 c.c. of the standard. **Figs. 7 and 8.** No. 45, B.M., age 31. Para V Gr. VI. Pregnancy of 19 weeks. HI = 30. A-Z reported negative. X-ray confirmed pregnancy.

Method.—The simplified method of determination of histaminolytic power of serum as outlined by Anrep and others, with slight modifications, was used in this investigation.

Control and test (active) samples of serum were assayed against a standard solution of histamine diphosphate, 0.5 micrograms to the c.c., on the atropinized guinea pig's ileum.

To one c.c. of the serum to be tested, 1 c.c. of a solution of histamine diphosphate, 3 mcgm. per c.c. in Tyrode's solution is added, mixed and incubated at 37° C. for 30 minutes. The sample is then rapidly diluted with 4 c.c. of Tyrode's solution and heated quickly to 80° C. for 5 minutes to stop further histaminolysis.

For the control sample, 1 c.c. of serum is diluted with 4 c.c. of Tyrode's solution and the temperature of the mixture raised to 80° C. for 5 minutes. After cooling, 1 c.c. of a solution of histamine diphosphate, 3 mcgm. per c.c., is added giving a final concentration of 0.5 mcgm. per c.c. This is then incubated for 30 minutes at 37° C., as is the test sample.

The test sample is then assayed against a standard solution of histamine diphosphate, 0.5 mcgm. per c.c. after the control sample has been compared with the standard solution. The assay was performed on the guinea pig's ileum in atropinized (0.5×10^{-6}) Tyrode's solution using a bath of approximately 20 c.c. volume which was emptied by overflow, suspended in a water bath at 37° C. The guinea pig was starved for 12 to 24 hours previous to the test, and the approximately 1 inch strip of ileum was placed for 30 minutes in the muscle bath prior to assay to permit recovery of sensitivity. Following this, the preparation was stimulated with doses of a standard solution of histamine diphosphate 0.5 mcgm. per c.c. which produced approximately 50% of the maximal response. This and all histamine solutions were freshly prepared prior to each day's assays. When contractions of equal height were produced by similar doses, the control solution was alternately compared with the standard solution in equal quantities. The heated diluted serum in the control frequently initially decreased the sensitivity of the ileum preparation, but sensitivity was usually regained following several contractions. If the control and standard solutions were not regarded as identical in response of the ileum to equal doses, the test was excluded. This only occurred in 2 cases, however, and in these excessive hæmolysis had occurred. As Anrep and others point out, even small concentrations of blood diminish the sensitivity of the intestine and its responses become erratic. When the control and standard were shown to produce equal responses to equal doses, the test solution was assayed against the standard solu-

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tion. All amounts of the solutions were mixed in the muscle bath by air and all were added at 2 minute intervals and left in contact with preparations for 30 seconds.

RESULTS

The following assays give an idea of individual results obtained and represent tracings of various ranges of histaminolytic power. In the series 5 controls were investigated, 3 male and 2 female, and no evidence of histaminolytic activity was found. This conforms with the findings of Anrep.

In addition, several interesting cases were investigated but not included in the series.

W.P., a 41 year old para 6, gr. 7 (or 8?), gave a history of having had her last menstrual period on January 12, 1948. Blood was taken for histaminase investigation on May 13, and assayed the following day. There was slight histaminase activity reported, but not consistent with a pregnancy of the duration of amenorrhœa. On June 15, the A-Z test was reported negative. The patient was referred to Gyn. clinic, where it was felt that she was experiencing the menopause. However, slight vaginal bleeding recurred in September and on the 15th of that month the patient returned to clinic presenting a mass of tissue which had been passed by vagina. Pathological examination showed this to be products of conception and a diagnosis of missed abortion was made.

TABLE I.

SUMMARY OF RESULTS
HISTAMINOLYTIC ACTIVITY IN SERUM IN PREGNANCY

Duration of pregnancy				
Weeks	*Lunar months*	*No. of cases*	*HI average*	*HI average (Anrep) app.*
0-4	1	0	—	—
5-8	2	1	15	—
9-12	3	2	30	24
13-16	4	4	34	34
17-20	5	6	58	47
21-24	6	5	73	58
25-28	7	6	78	67
29-32	8	5	84	75
33-36	9	4	79	82
37-40	10	14	92	92
Total		47		

One case of severe pre-eclampsia was investigated at 37 weeks' duration of pregnancy, and showed an HI of 60, considerably below the average of the tenth lunar month of 92.

In only one case in the series was an HI which showed no activity in a case of proved pregnancy obtained. This was in a 19 year old primipara at 13 weeks and unfortunately, no repeated test was made.

DISCUSSION

The results obtained in this small series show considerable agreement with those of Anrep *et al.* The case of 8 weeks' duration subsequently aborted and probably should not be included in the series, since all the other cases were followed through to term and the duration of pregnancy calculated rather than merely estimated on clinical grounds at the time of taking the sample. Any case that lacked this follow-up was not included in the series.

The HI in this series tends to be slightly higher than those of Anrep *et al.*, but the trend is certainly similar, showing an increase in HI from the beginning of the third lunar month, progressing to term. The slight decrease shown in the ninth lunar month would not appear to be significant, within the limits of error of the test.

In addition, normal male and female serum showed no histaminolytic activity.

CONCLUSION

1. Five specimens of human sera, 3 normal male, and 2 normal female, showed no histaminolytic activity under the testing procedure used.

2. In pregnancy, histaminolytic activity is greatly increased, beginning certainly as early as the tenth week, and increasing to reach a maximum close to term.

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TUBERCULOUS EMPYEMA COMPLICATING ARTIFICIAL PNEUMOTHORAX*

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THE TREATMENT of tuberculous empyema complicating artificial pneumothorax is still a most controversial subject. In the current literature two main schools of thought exist. On the one side authors, such as Houghton[1] recommend the immediate discontinuance of an artificial pneumothorax as soon as the fluid effusion containing tubercle bacilli appears. Most of these writers conclude that washouts and instillations of the different bacteriostatic and bactericidal substances are of no value.

This attitude is not justified today. We have powerful antibiotics and bacteriostatic agents. It is definitely illogical to give up a good artificial pneumothorax just because some tubercle bacilli have been found in a liquid effusion. It is further illogical to presume, that a substance like streptomycin, PAS or the thiosemicarbazones (Tb I especially) should not act in a pleural space, where we can apply them in doses and concentrations which will not permit any tubercle bacilli to live longer than a few days or hours. If we have bad results with these drugs it is not due to the ineffectiveness of the drugs but rather to our wrong and ignorant application. It is not that the drug is ineffective, but that the treatment is insufficient. The logical development of modern treatment with antibiotics and bacteriostatics is to bring the drugs in direct contact with the germ as much as possible. In other words we must permit the drug to reach any part of the space we want to treat. 10 to 100 c.c. (maximum) of liquid containing the drug, will not assure a continuous contact of each part of a pleural cavity with a volume of 500 to 2,000 c.c. or more. The purpose of this article is to show how the bacilli from even long standing tuberculous empyema can disappear within a few days.

A review of the literature shows that beside Houghton[1] quite a number of other writers are of the opinion that the conservative treatment is not efficient and that immediate surgery is the method of choice. Recently Cuthbert[2] expressed this point of view, recommending early surgery as the method of attack. He discusses at great length the literature dealing with this subject.

On the other hand the number of authors who saw good results from the conservative treatment is large and in the last years even increasing. Arnold,[3] Bernard and co-workers,[4] Bindslew[5] and other writers report very favourable results with streptomycin-treatment in local application to tuberculous empyema. Only after completing this article we found Bindslew's paper, who reports in 1949 his results in treating tuberculous empyema in the same manner as we are describing here in this article. He saw in all his cases the same rapid improvement which we have seen in our cases too. But Smith[6], Dijkstra[7] and others, have not seen the same good results, and are more sceptical concerning the value of streptomycin. Lehmann,[8] Vallentin[9] and others claim uniformly good results from the local treatment with PAS. Koch,[10] Malluche[11] and other writers have seen very good results from the local treatment with Tb I. Malluche even says that the healing of a tuberculous empyema should not offer a problem any more today. Lastly there are many writers, especially in the older literature, who have seen very good results from conservative treatment in tuberculous empyema.

Ole Christensen,[12] in the most recent literature reports excellent results treating acute tuberculous empyema with streptomycin in a large amount of saline.

MATERIAL AND METHODS

The term tuberculous empyema is used after the definition of Jones and Alexander,[13] namely: "purulent pleural effusion containing tubercle bacilli with underlying tuberculosis of the lung or pleura". Furthermore we have applied this definition only to cases where tubercle bacilli have been found more than once in a pleural effusion.

We have reviewed the artificial pneumothorax cases of the Waldsanatorium, Davos, from October 1945 to October 1950. Only cases that have been under observation and treatment for more than three months have been considered. The observation periods for the different cases are as follows:

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*This article was written at the Waldsanatorium, Davos, Switzerland.

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TABLE I.

Months of observation	*Number of artificial pneumothoraces*	*% of the total of cases*
3 - 6	17	11
7 - 12	37	24
13 - 24	41	26
25 - 36	32	21
Over 36	28	18
Total number artificial pneumothoraces		155
Total number of patients		137
Total number of Jacobaeus operation		102

Of the total number of the artificial pneumothoraces 101 or 65% have been observed for more than one year. Only 69 (44.5%) of the 155 have been complete, the rest being more or less incomplete. 13 cases of tuberculous empyema occurred (8.4%), all in cases with incomplete artificial pneumothorax. Four of the 13 cases arrived with the complication, the rest developed it during treatment here. Three patients developed empyema as a consequence of a bronchopleural fistula, in two cases after a Jacobaeus operation and in one case as a consequence of the progressive disease.

In a series of 14 extrapleural pneumothoraces observed over a period of 4 to 22 months, two patients developed nontuberculous infection of the pleural cavity. Both cases treated in the new way became sterile in a very short time.

TREATMENT

Of the 13 cases of tuberculous empyema, 4 were treated surgically, and one died of progressive tuberculosis without any special treatment, and 8 were treated conservatively.

Of the 4 patients treated surgically, three had a broncho-pleural fistula, which was proved by one of the known clinical methods. Two of these patients died after thoracoplasty, one with fistula, one without. These fatalities were due more to the patients' toxic condition as a consequence of the empyema than to the underlying tuberculosis.

Of the 8 remaining patients, treated with pleural washouts, none died. One patient left us during treatment, the other 7 have been cured. We consider a patient as cured, when we could not detect any tubercle bacilli in the withdrawn fluid in antiformin concentration. This was considered as permanent when the result was the same in 4 consecutive weeks. In three of these cases the collapse of the lung was maintained and the pleural cavity is now dry. In three other cases an oleothorax was induced with good results. In one case the re-expansion of the lung was attempted but not achieved. A first stage thoracoplasty was done with good result, the pleural cavity remained sterile.

A mixed infection was existing in three of our cases at some time during the treatment and was cured. No special attention is drawn to this kind of complication, as the treatment is the same as for tuberculous empyema but with other substances.

In 4 of our cases the treatment was done in the normal way with one, two or three washouts per week, depending on the severity of the case. In these cases the final good result was achieved after several months. For washing the pleural cavity we used: physiological saline solution, Jessen's solution, azochloramid and gentian violet, the two latter drugs for combating mixed infection. Since we have had PAS, Tb I and streptomycin we left in these cases some saline solution—not more than 100 c.c.—in the pleural space, adding the tuberculostatic agent. With this procedure sterility of the pleural space was achieved only after months. In the other three cases we applied a new routine which gave us much better results, and this will be described with reference to one particular case. Furthermore we have had lately the occasion to treat two other cases (one with a very small bronchopleural fistula) of empyema in the same way, so that we have in all 10 cases, of which 5 have been treated with the new routine, with precisely all the same excellent result.

EXAMPLE OF NEW WASHOUT ROUTINE

The patient was suffering from a cavitating tuberculosis of the right lung. An artificial pneumothorax and an extrapleural pneumothorax were ineffective. In a third operation both spaces were combined, thus producing a total collapse of the diseased lung. As a result of this operation the patient developed a heavy tuberculous empyema and an external fistula in the operation scar. At the first puncture the pus was found to be heavily positive for tubercle bacilli in the direct examination. We then started the patient on washouts every second day. The first task was to close the external sinus. In order to do this we advised the patient to stay in the sitting position or to lie on his left side, so that the sinus could not be reinfected by pus trickling through it. After each washout we left 2 to 300 c.c. of liquid in the pleural cavity containing PAS, Tb I, or Tb VI. The amount of liquid left in the pleural space was just enough, not to reach the height of the sinus, if the patient kept in his sitting position. At the same time we treated the sinus locally with Tb I and PAS. In conjunction with this local treatment the patient was treated with streptomycin by injection, PAS and Tb I by mouth. No unpleasant reaction occurred. The amount of PAS left in the pleural cavity was each time 8 to 10 gr., Tb I 0.5 to 1.0 gr., and Tb VI up to 5 gr. In order not to produce a resistant germ, we did not use streptomycin in the local treatment. The other three

drugs were used alternatively. After 6 weeks of treatment the sinus was closed. At this time only very few tubercle bacilli could be detected in the fluid withdrawn from the pleural cavity. After the sinus had been closed we left in the pleural space 4 to 500 c.c. of liquid containing the said quantity of drugs. After another 6 weeks no bacilli could be found in the fluid any more. The last washout was done 4 months ago. No relapse has occurred. The artificial pneumothorax is dry and maintained. The underlying tuberculosis of the lung is clinically cured, the cavity being closed tomographically.

During the whole time of treatment the urine and the blood were controlled and no pathological changes could be seen. In two other cases of our material we applied the same routine with the same good results.

THEORETICAL CONSIDERATIONS

Petroff and co-workers showed in a most interesting article that body fluids can stop completely or partially, the action of bacteriostatic or bactericidal substances. This mechanism is known for streptomycin and PAS too. Streptomycin does not act in an acid milieu. We know that streptomycin, PAS and Tb I make life impossible for tubercle bacilli from a certain concentration on. Therefore, as in the *in vitro* experiment, we must be able to kill any germ in the pleural space, providing the drug is in continuous contact with every part of the pleural space. These conditions are attained if we introduce into the pleural cavity at least 500 to 600 or even more c.c. of liquid containing a sufficient concentration of PAS, Tb I or streptomycin. If the pleural space is smaller, we can fill it completely with liquid, thus assuring a continuous contact of the active substance with every part of the cavity. In these cases we have almost the ideal conditions of the *in vitro* experiment. In an older empyema the walls are thick and little or no communication between the body and the empyema cavity exists. This, originally the reason for the difficulties in combating this complication is today our help. It enables us to give doses of bactericidal substances in the pleural space that would be toxic if given under other circumstances. This explains the fact that we have never seen any ill effects from single doses of 1.0 gr. of Tb I, which always have been very well tolerated.

Another question of theoretical interest is whether it is desirable to maintain an artificial pneumothorax with the complication. Each case must be judged on its own merits, depending on the lung condition, but generally speaking a good working artificial pneumothorax should not be given up. Normally the patient with the tuberculous empyema is in bad general condition, and a larger surgical intervention is not possible. Successful treatment of the empyema if often the key for further treatment. The general condition must be improved first. In our experience it seems clear that through a rational treatment of the empyema a large percentage of patients can be cured without any surgical intervention. But in those cases where surgery becomes necessary, the risk of operation is greatly diminished through this treatment.

SUMMARY

A review is given of tuberculous empyema occurring during a period of 5 years from 1945 to 1950 at the Waldsanatorium, Davos, Switzerland. During this time 155 artificial pneumothoraces were observed for periods of three months to several years. 13 cases of tuberculous empyema occurred, *i.e.*, 8.4%.

It is concluded that the best treatment is the conservative treatment, provided that the cases are not complicated by larger broncho-pleural fistulas. This treatment gives us the opportunity of avoiding surgery altogether or postponing it until a more opportune moment. Most of the cases were negative for tubercle bacilli in the withdrawn fluid after one to two weeks. It is noted that by introducing into the pleural cavity at least 4 to 600 c.c. or even more of an isotonic PAS, Tb I, streptomycin or Tb VI solution, the result of the treatment is rapid. Tubercle bacilli disappear after two or three washouts in the liquid. Smaller pleural cavities can be filled completely with liquid. It is thus assured that every part of the pleural space is continuously washed with the tuberculostatic agent. It is emphasized that in most of these cases major surgery can be avoided altogether.

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Further literature can be obtained from the author.

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GLUCOSE METABOLISM IN ANXIETY STATES*

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THERE HAVE BEEN many attempts to demonstrate a correlation, at a given time, between the glucose level of the blood and the emotional state of a subject under examination. However with the exception of the hyperglycæmic reaction common in acute anxiety, anger, and fear, no constant relationship between emotion and glycæmia has been established.

Glucose tolerance studies in the psychoneuroses have engaged the attention of many investigators since Langston[1] in 1922 reported an excessive hyperglycæmic reaction in neurasthenia. Although the work of Olmstead and Gay[2] was in apparent agreement with that of Langston, the expected rise in blood sugar after glucose ingestion by neurasthenic subjects could not be obtained by Szondi and Lax.[3] That their neurasthenics were not ordinarily hypoglycæmic was shown by comparing the post-absorptive blood sugar levels in psychoneurotic and normal subjects and finding them identical. According to Steven,[4] Dorst in 1937 found that persons with neurocirculatory asthenia manifested increased glucose tolerance and that a relatively flat curve was obtained in neurasthenic subjects in general. This led him to express the view that the low blood sugar levels were responsible for the symptoms in his neurotic subjects. Steven confirmed these findings but could not agree that the low blood sugar was solely responsible for the asthenia, since some of his patients did not have low values and none of the symptoms were relieved by sugar feeding. Moreover one patient had an accompanying diabetes mellitus with hyperglycæmia.

Peskin[5] described a symptom-complex simulating peptic ulcer, neurocirculatory asthenia and psychoneurosis, and expressed the opinion that increased sugar tolerance was a factor in the production of the complex. He considered that patients in this group would display symptoms of mild hypoglycæmia at relatively high blood sugar levels. Finally Portis and his associates[6, 7] have reported the coincidence of a flat glucose tolerance curve with fatigue states, which they ascribe to liberation of increased amounts of insulin due to vagal stimulation of the pancreas by emotional impulses. The vague and contradictory nature of the evidence regarding glucose metabolism in psychoneurotic states and the lack of unanimity in the interpretation of the reported results, suggested that an adequately controlled study of glucose tolerance utilizing the most modern techniques, in a carefully chosen group of psychoneurotic patients, might be of value.

CHOICE OF SUBJECTS

The patients selected for this study were carefully chosen from a group of undoubtedly psychoneurotic subjects, as those exhibiting in a marked degree symptoms directly attributable to anxiety. As the basis for this selection, we have adopted the definition of anxiety as enunciated by Cleghorn and Graham.[8] "Anxiety is generally recognized as a condition of tense preparedness for action or a state of tension aroused by a sense of impending danger." These authors further state that anxiety becomes an abnormal reaction only when precipitated by ordinarily insufficient agencies or when it is present in the absence of contemporary stimuli.

The problem of classification of the psychoneuroses continues to plague psychiatrists and it should be understood that our use of the term "anxiety state" does not imply that these patients can be considered separately from other psychoneurotic types. Most of the patients showed symptoms other than the nervousness and irritability attributable to anxiety. Fatigue was a very prominent symptom in the group and the usual pattern was that of great fatigue on awakening in the morning which improved somewhat as the day progressed. Insomnia, dizziness, lightheadedness, tension and depression were less frequent manifestations. The psycho-pathological process in these anxious patients was a chronic one and every effort was made during the testing to avoid precipitating an acute anxiety reaction due to concern over needling of veins and drawing of blood. Reassurance was freely given and diversion attempted in each patient during the tests.

The control groups were obtained from healthy medical students and interns who had volunteered to assist in this investigation, supple-

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mented by ambulant patients hospitalized for ailments which would not be expected to influence glucose tolerance (*e.g.*, varicose veins of the legs, inguinal herniæ).

All were carefully investigated and only those selected who showed no signs of an anxiety condition, before, during, or after the glucose tolerance tests. These tests were carried out only after the subject had been on the standard hospital diet of approximately 80 gm. protein, 130 gm. fat, and 300 gm. carbohydrate for a minimum of four days. None of the subjects received any medication and all were in a good state of nutrition.

Finally a small group of both the neurotic and control subjects were subjected to repeated oral glucose tolerance tests in an attempt to determine the so-called "spontaneous variability" of the test. We do not propose to present the detailed results of this study at the present time. It was however apparent that there was sufficient coincidence to enable us to exclude this factor as a significant agency contributing to misinterpretation of the results.

TECHNIQUES

Blood glucose analyses were performed by the method of King and Garner,[9] designed to give true glucose values. Oral glucose tolerance tests were performed in the usual manner. The dosage consisted of 50 gm. glucose in 250 ml. of water and this was followed by serial blood and urine studies, in all cases for three hours, and in as many as possible, for five hours.

Intravenous glucose tolerance tests were performed on approximately half the subjects who had been submitted to the oral test. There have been numerous techniques proposed for the performance of this test and these have generally taken the form of either a rapid infusion of a concentrated solution of glucose or a slower infusion of a more dilute solution. The latter method was adopted in this study.

Since the patients dealt with did not vary to a great extent in body weight, in all cases a standard dose of 350 ml. of a 10% solution of glucose (35 gm.) was administered over a period of 20 minutes, and serial samples of blood taken and analyzed.

Finally, a group of the patients who had been subjected to the oral test were also subjected to an insulin-glucose tolerance test in order to discover their sensitivity to insulin and their response to insulin-induced hypoglycæmia, if such occurred.

At least three different methods have been advocated for the study of the varying responses of the body to parenteral insulin administration. These are: (1) the intravenous administration of insulin alone (insulin tolerance test); (2) the simultaneous administration of glucose orally and insulin intravenously (glucose-insulin tolerance test); (3) the administration of insulin intravenously followed by glucose ingestion after 30 to 60 minutes, or when the first symptoms of hypoglycæmia appear (insulin-glucose tolerance test). The latter test, described by Engel and Scott,[10] was chosen for this study. The details are as follows:

In the morning after a 12 hour fast venous blood was withdrawn and analyzed. Then 0.1 units Toronto Insulin (Connaught Laboratories) per kg. body weight was injected intravenously. After 30 minutes or when the first symptoms of hypoglycæmia appeared (whichever was first) 50 gm. glucose were given by mouth. Blood samples were taken at 30 minutes (immediately prior to the administration of glucose) and at 60, 90, 120 and 180 minutes from the start of the test. For purposes of analysis and comparison with other studies blood sugar levels were expressed as a percentage of the initial blood sugar. All blood samples were collected in fluoride and oxalate. Repetition of tolerance tests was done only after a minimum interval of four days had elapsed.

RESULTS

Comparisons of the data obtained on psychoneurotic and control subjects in the performance of the oral glucose tolerance test, the intravenous glucose tolerance test, and the insulin-glucose tolerance test, are presented in Tables I, II, and III respectively. Statistical comparison of the mean values of the blood sugar at the given time intervals was obtained by applying the t-test to the data. The results of this comparison have been indicated in the column headed P_t. The average curves obtained in the performance of the respective tests are seen in Figs. 1, 2, and 3.

The results of some 70 separate estimations of fasting blood sugar on 36 psychoneurotic subjects indicated that there was no significant difference between the mean values of these patients and those of the control groups. Moreover the range of values of the neurotic group was within the usually accepted normal limits.

Following the introduction of glucose into the body either through the gastro-intestinal tract or by vein, however, the blood sugar values indicated for the majority of the psychoneurotic group, a tolerance for glucose greater than that of the corresponding controls, and this was irrespective of the route of administration.

In the case of the oral test there was a highly significant difference at one-half hour, a significant difference at one hour, but no significant difference at either two, three, four, or five hours. There was no suggestion of hypoglycæmia at

four or five hours in either the control group or in the psychoneurotic subjects.

In the intravenous tests the situation was similar. The fasting blood sugar values were normal in both groups but at ten minutes from the start of the infusion there was a significantly lower mean value in the psychoneurotic group and at twenty minutes a highly significant lower mean value in this group. At forty minutes the mean level of the psychoneurotic was still significantly lower than that of the normal group. During the next thirty minutes the two curves approached one another and no significant difference in the mean levels was apparent at 70, 100, or 130 minutes.

In the case of the insulin-glucose tolerance test, the neurotic group responded with approximately the same depression of blood sugar as the normal group after insulin administration. Thus insulin "sensitivity" was the same in the two groups. One hour after drinking the glucose the mean level of the psychoneurotic group was significantly lower than that of the control group, but at two and three hours no significant difference existed.

DISCUSSION

From the reported results it is evident that the patients chosen for this study, *i.e.*, people suffering from a psychoneurosis characterized mainly

TABLE I.

ORAL GLUCOSE TOLERANCE TESTS IN PSYCHONEUROTIC SUBJECTS AND CONTROLS

PSYCHONEUROTIC GROUP						CONTROL GROUP				
Minutes after administration	*No. of subjects*	*Mg. glucose per 100 ml. blood* *Max.*	*Min.*	*Av.*	P_t	*Minutes after administration*	*No. of subjects*	*Mg. glucose per 100 ml. blood* *Max.*	*Min.*	*Av.*
0	36	103	67	84	P>0.05	0	12	97	78	87
30	36	140	80	112	P<0.01	30	12	157	110	140
60	36	135	70	104	P<0.05 P>0.01	60	12	160	73	123
120	36	115	58	75	P>0.05	120	12	125	67	85
180	36	105	53	80	P>0.05	180	12	100	53	80
240	16	107	67	81	P>0.5	240	10	103	70	83
300	16	110	67	87	P>0.30 P<0.40	300	9	103	80	91

TABLE II.

INTRAVENOUS GLUCOSE TOLERANCE TESTS IN PSYCHONEUROTIC SUBJECTS AND CONTROLS

PSYCHONEUROTIC GROUP						CONTROL GROUP				
Minutes after injection	*No. of subjects*	*Mg. glucose per 100 ml. blood* *Max.*	*Min.*	*Av.*	P_t	*Minutes after injection*	*No. of subjects*	*Mg. glucose per 100 ml. blood* *Max.*	*Min.*	*Av.*
0	18	88	75	75	P>0.05	0	11	91	64	75
10	12	176	114	152	P<0.05 P>0.02	10	8	191	130	178
20	18	231	152	199	P<0.01	20	11	273	211	231
40	18	184	98	134	P<0.01	40	11	202	114	163
70	18	156	60	90	P>0.05	70	11	131	48	88
100	18	96	46	66	P>0.50	100	11	91	50	67
130	18	113	44	68	P>0.50	130	11	89	44	65

TABLE III.

INSULIN-GLUCOSE TOLERANCE TESTS IN PSYCHONEUROTIC SUBJECTS AND CONTROLS

PSYCHONEUROTIC GROUP						CONTROL GROUP				
Minutes after injection	*No. of subjects*	*Glucose per cent of fasting blood sugar* *Max.*	*Min.*	*Av.*	P_t^1	*Minutes after injection*	*No. of subjects*	*Glucose per cent of fasting blood sugar* *Max.*	*Min.*	*Av.*
30	16	91	20	49	P>0.5	30	10	75	22	46
60	16	146	49	94	P>0.2 P<0.3	60	10	142	73	107
90	15	151	84	100	P>0.01 P<0.02	90	10	191	86	130
120	16	186	76	115	P>0.5	120	10	188	73	123
180	14	156	59	103	P>0.5	180	10	158	79	107

by chronic anxiety, manifested an increased tolerance for orally and parenterally administered glucose, and gave an unsatisfactory response to insulin-induced hypoglycæmia. This is in line with the findings of Dorst, Portis and others, but the data now submitted are not in accordance with the various explanations advanced to account for this anomaly.

An apparently increased tolerance can result from many causes: general malnutrition or the lack of one or more dietary factors; inefficient absorption of glucose from the digestive tract; adrenal cortical or pituitary insufficiency; hypothyroidism; and hyperinsulinism.

The method of selection of the patients, and the fact that they and the controls were all placed on the same ample standard hospital diet before testing serves to eliminate any nutritional

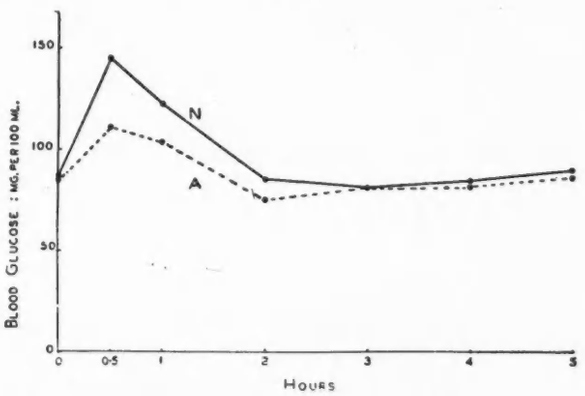

Fig. 1.—The oral glucose tolerance curve in normal (N) and psychoneurotic (A) subjects: mean values.

factor as the cause of the increased glucose tolerance. That it was not due to slow or faulty absorption from the intestinal tract became evident when it was seen that intravenous administration of glucose resulted in much the same degree of increased tolerance as when the glucose was given orally. Moreover after the oral test, 77% of the patients showed a return to the fasting level or even lower in two hours. The absence of glycosuria during the oral test also eliminates the possibility of a renal factor. None of the patients showed any clinical symptoms indicating adrenal, pituitary or thyroid insufficiency. Further the normal fasting blood sugar levels, normal insulin "sensitivity", and absence of an exaggerated hypoglycæmic response to either the oral or intravenous glucose tolerance test seems to rule out disorders of the adrenal and pituitary glands, while the increased intravenous tolerance and the probable absence of faulty absorption militates against hypothyroidism.

We are left then with hyperinsulinism as a possible explanation, and it should be noted that this is the theory advocated by Portis in a recent paper in which he found that 157 patients with fatigue as an outstanding or unexplained symptom showed an average intravenous glucose tolerance curve which was "flat" in comparison with the average curve of 772 controls. Portis postulated that in these psychoneurotic patients long continued stimulation of the fibres of the right vagus nerve could result in liberation of increased amounts of insulin, and pointed out that a certain proportion of his "fatigue" patients

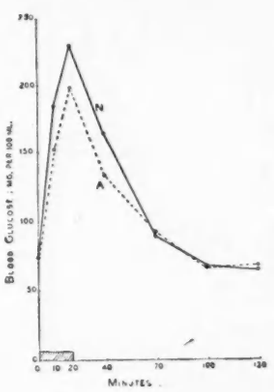

Fig. 2

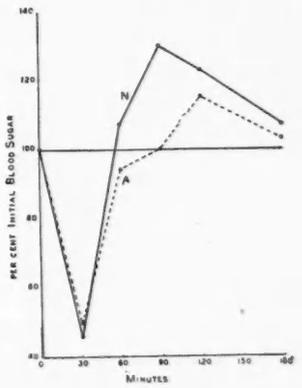

Fig. 3

Fig. 2.—The intravenous glucose tolerance curve in normal (N) and psychoneurotic (A) subjects: mean values. The cross-hatched area represents the duration of the intravenous infusion. **Fig. 3.**—The insulin-glucose tolerance curve in normal (N) and psychoneurotic (A) subjects: mean values expressed as percentages of the initial (fasting) blood sugar.

showed a tendency towards a normal response when the glucose tolerance test was performed after administration of 1/50 gr. of atropine.

The number of cases we have investigated is small in comparison with those of Portis, and it is a question whether what we have characterized as an "anxiety state" is strictly comparable with the "fatigue" syndrome exhibited by his patients. Nevertheless the correspondence is sufficiently close that the same argument should be valid for both series. We were however unable to accept hyperinsulinism as an explanation for our observed results. None of our cases showed a fasting hypoglycæmia after glucose administration even in the five hour oral test. Moreover none of the patients subjected to the insulin-glucose test exhibited any excessive sensitivity to insulin, as might be expected in cases of hyperinsulinism. On the theoretical side the hyperinsulinism hypothesis pre-supposes vagal

stimulation as a factor in glucose metabolism, and the rôle of the vagus in this connection is at best controversial. According to Jensen,[11] the strongest evidence in favour of vagal control of insulin secretion, that of LaBarre and his associates, has been disputed by Gayet and Guillaumie who were unable to confirm the findings upon which LaBarre based his claims; while the established fact that glucose metabolism pursues an apparently normal course in an animal with a denervated pancreas (Houssay[12]) is not in agreement with a hypothesis of vagal control. Moreover Adams[13] has reported recently that intravenous glucose tolerance tests before and after vagotomy for duodenal ulcer, showed no significant differences. We were therefore obliged to look elsewhere and the following tentative hypothesis is advanced as a possible explanation of our results.

It has been established that in anxiety states the work of certain tissues is increased. Hickam and collaborators[14] have shown that anxiety increased the pulse rate, the blood pressure and the cardiac output. The presence of irritability, tension, tachycardia and tremulousness in these patients almost certainly calls for increased energy production to sustain the hyperfunctioning heart, musculature, and perhaps other tissues although evidence for the latter is scanty.

It is postulated that in the psychoneurotic patients, in the resting state, the increased requirements of certain tissues are met by acceleration of the hepatic glycogenolytic process with maintenance of normal levels of blood sugar at the price of a temporary but relatively large decrease in the glycogen stores of the liver. With the introduction of exogenous glucose, the immediate response is to restore the supply of liver glycogen in preparation for future demands. This results in a diminished supply of sugar immediately available to the blood stream, and consequently lower blood sugar curves, no matter what the avenue of introduction of the sugar. When a satisfactory equilibrium is established the glucose tolerance curve assumes its normal shape. The normal liver, since it is not subjected to so great a functional strain does not remove glucose so rapidly. The basic tenet of this theory is, then, that in the psychoneurotic there is an exaggeration of the normal ebb and flow of hepatic glycogen stores, due to the demands of certain extra-hepatic tissues. The explanation of the failure to respond with hyperglycæmia after glucose ingestion in the insulin-glucose tolerance test is also found in depleted hepatic glycogen stores.

Some support for this theory has been found in the work of Hinkle and colleagues[15] on the relation of stressful life situations to the concentration of ketone bodies in the blood of diabetics and normal individuals. These investigators found that stressful stimuli in the normal and in the diabetic individual were capable of producing a rise in the ketone-body content of venous blood. They further showed that when emotional security was achieved the level subsided. Mirsky[16] believes that the essential stimulus to ketone formation by the liver is a decrease in liver glycogen and this belief is generally regarded as at least a partial explanation of ketosis. It follows that if the hypothesis of greatly fluctuating glycogen be accepted, the explanation of the moderate rise in ketone bodies in Hinkle's patients is facilitated. Conversely, the demonstration of a mild ketonæmia in these patients is indirect evidence in favour of the hypothesis of greatly fluctuating stores.

SUMMARY AND CONCLUSIONS

1. A study of tolerance for orally and intravenously administered glucose was performed on a group of patients who were suffering from a psychoneurosis, the principle feature of which was anxiety. The same patients were tested with the intent of discovering their glycæmic reaction to intravenously administered insulin and their response to insulin-induced hypoglycæmia, if such occurred. All studies were controlled.

2. The patients dealt with in this study manifested an increased tolerance for glucose administered by mouth or parenterally.

3. The patients further manifested a normal response to the hypoglycæmic action of insulin but did not respond with a satisfactory elevation of blood sugar when glucose was administered orally during the period of hypoglycæmia.

4. The observed abnormalities are explained by the tentative hypothesis that there is increased utilization of glucose by certain tissues and compensatory increased hepatic glycogenolysis.

We desire to express our indebtedness to Dr. J. D. Adamson, Chief of Medicine, Deer Lodge Veterans' Hospital, for his keen interest in the problem, and to Dr. G. E. Delory of the Department of Biochemistry, University of Manitoba for many helpful suggestions.

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ACTH IN ASPIRATION OF PEANUTS

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Since the general practitioner or pædiatrician is usually the first to encounter children who have aspirated foreign bodies we wish to commend their diagnostic ability in the early recognition of these cases. Fortunately peanut aspiration into the lung is an infrequent occurrence in adults 90 to 92% occurring in young children according to those who have greater experience.

The difficulties encountered during and after the removal of a peanut from the lungs of these young children prompted us to attempt a new approach to the problem. The small size of the larynx and trachea at this age restricts one to the use of a 3.5 to 4 mm. bronchoscope with attending mechanical difficulties and often requires a tracheotomy subsequently to relieve the subglottic œdema which invariably occurs. The seriousness of the child's condition varies with degree of obstruction, the age of the patient, and the allergic response of the patient's bronchi to the peanut. The reaction in the bronchial tree is characterized by marked œdema of the bronchial mucosa and profuse secretion. Bonnier claims that this reaction is due to mechanical irritation. Others believe the reaction to be due to allergic reaction on the part of the bronchial mucosa to oils found not only in peanuts but other edible nuts as well. Whichever explanation is correct the fact remains that the violent reaction is so intense that urgent attention is required. The possibility that the reaction observed could be allergic in nature prompted us to attempt the use of ACTH in a recent case.

Case Report

A young male child aged 2 years was referred by Dr. Morley Cody, on May 29, 1951. Three hours prior to admission the child was reported to have choked while eating peanuts. His obstructive symptoms were marked. Direct laryngoscopy showed sub-glottic œdema so advanced that a bronchoscope could not be passed. A tracheotomy was then performed under local anæsthesia. Due to the patient's condition no further attempt was made to remove the peanut at this time.

On May 30, radiographic examination of the chest disclosed atelectasis of the right upper lobe. Bronchoscopic examination through the tracheotomy wound revealed marked œdema of the mucous membranes of the bronchi. There was also marked secretion. No foreign body could be visualized. Despite aspiration of the bronchial tree through the bronchoscope the patient showed marked cyanosis and his condition remained poor.

On May 31, the child was given ACTH, receiving 6 intramuscular injections of 10 mgm. each. Due to the continuing obstructive symptoms at the onset of therapy with ACTH, adrenalin 1 in 1,000 in ½ c.c. doses was instilled into the tracheotomy tube prior to aspiration of the bronchial tree. This produced only slight relief. At the onset of ACTH therapy the breath sounds were absent over the entire left chest. Bronchoscopy was repeated 6 hours after the first dose of ACTH. The mucous membrane of the bronchi was no longer œdematous and the secretion was scanty and thick. During this examination a quarter of a peanut was clearly visualized in the left main stem bronchus and was easily removed. After aspiration of the bronchial tree the breath sounds returned to the left chest and the patient's condition improved rapidly.

On June 1, respiratory difficulty continued intermittently with but little secretion being obtained on aspiration through the tracheotomy tube. Bronchoscopy was repeated at 2 p.m. to remove crusts from both main stem bronchi. The ACTH was discontinued because of this finding. By 6 p.m. the patient was again cyanosed and semi-conscious. The pupils were dilated. Coarse râles were heard over both lungs. Continued suction with the use of adrenalin intra-tracheally produced some relief. The secretion had again become profuse. The child was again placed on ACTH 5 mgm. every six hours for 3 doses.

The general condition was much improved on the next day and from then on recovery was uninterrupted. The ACTH was discontinued on June 3 and the tracheotomy tube was removed on June 8 without incident.

On June 11, the child was discharged at which time the tracheotomy wound was closed and the chest was entirely clear on physical examination.

In the present problem where one is confronted with an extremely serious situation any assistance of even doubtful value is readily accepted by the bronchoscopist. The reaction in the bronchial tree which results from the inhalation of a peanut is so intense and so rapid that drastic measures are required to save the life of the patient. There appears to be some debate

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as to whether the reaction in the bronchial tree is purely mechanical or is the reaction of an allergic shock organ. The fact that peanuts are notoriously irritating to the bronchial tree led us to consider the possibility of allergy as likely possibility in the present case. On the basis of experience with this one case it would seem advisable to consider the use of ACTH or cortisone in additional cases of this type. It may be that one of these hormones should be used as soon as the possibility of inhalation of a foreign body is suspected in order that the bronchoscopist can have a more adequate opportunity of visualizing the entire bronchial tree without being seriously hampered by severe sub-glottic œdema and hypersecretion which is so intense that adequate exploration of the bronchial tree for the offending agent is impossible.

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CASE REPORTS

FIBRIN BODY IN THE PERITONEAL CAVITY DURING PNEUMOPERITONEUM THERAPY*

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OPAQUE SHADOWS in the pleural space are not uncommonly found during the course of pneumothorax therapy. These shadows are usually interpreted as fibrin bodies. Fleishner[1] first reported, in 1922, their occurrence in a patient receiving pneumothorax. Since then they have been reported by many other observers, both on the roentgenogram and through the thoracoscope in the living patient.

There are several theories concerning the origin of these fibrin bodies. By some they are thought to be agglomerations of fibrin from pleural fluid. Zavod[2] reports a case which came to autopsy that would seem to bear out this mode of origin. Maendl[3] subscribes to the same theory. He believes them to be due to end-products of the exudate which developed during pneumothorax treatment. Stöffel[4] thought they were due to deposits of fibrin around a nucleus of some sort. The most common nucleus was felt to be part of an adhesion torn during refill. Düll,[5] Klinkowstein and Belajeva,[6] Sachs[7] are inclined to the hæmic theory believing that a vessel is injured during pneumothorax refills and blood fibrin settles out in the hollow pleural space. Fibrin bodies have been reported in extrapleural pneumothorax as well. Oatway[8] reported two such cases of fibrin bodies.

Up to the present, no case of fibrin body in the peritoneal space during pneumoperitoneum treatment has been reported. One such case has come under our observation.

The patient, a white male, thirty years of age, was admitted to the Mount Sinai Sanatorium October 24, 1946 with a diagnosis of pulmonary tuberculosis, bilateral, moderately advanced, sputum was positive for acid fast bacilli. He was treated with left pneumothorax from June, 1946 to February, 1948 when, due to adhesions, pneumothorax was discontinued.

In an effort to attain conversion of sputum, a left phrenicotomy was performed on March 1, 1948 and pneumoperitoneum was induced on April 12. An opaque shadow was observed on the x-ray in the left upper quadrant, for the first time, on October 14, six months after pneumoperitoneum was instituted. In subsequent x-rays this shadow diminished in size and shifted in position. A series of x-rays showing the character and location of the shadow is reproduced.

June 28, 1950 peritoneoscopy was performed. Following is the report: The mass which was seen on the x-ray was found. It was situated on the posterior aspect of the anterior abdominal wall on the left side in the region of the needle punctures for the therapeutic pneumoperitoneum. This mass was about the size of a large walnut, reddish-brown in colour and in areas it was marbled with yellowish streaks. It was fixed to the abdominal wall and had all the appearances of an organizing hæmatoma. Impression: Hæmatoma, left upper anterior abdominal wall.

SUMMARY

A case of so-called fibrin body in the peritoneal space during pneumoperitoneum therapy is presented. This is the first such case reported in the literature. From our observations it would seem that this body was a hæmatoma probably due to rupture of a small blood vessel during a refill treatment.

*One of the exhibits of the Annual Fall Clinical Convention (1950) of the Montreal Medico-Chirurgical Society, Section of Tuberculosis and Diseases of the Lungs.

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CONCLUSION

"Un cas appelé corps fibreux dans l'espace péritonial durant un traitement de pneumopéritoine est présent. C'est le premier cas rapporté dans la littérature. D'après nos informations il semble que ce corps est un hématome probablement dû à une rupture d'un petit vaisseau sanguin durant un traitement de remplissage."

I wish to express my sincere thanks to Dr. M. Aronovitch, Consultant of the Mount Sinai Sanatorium, for performing and interpreting the peritoneoscopy.

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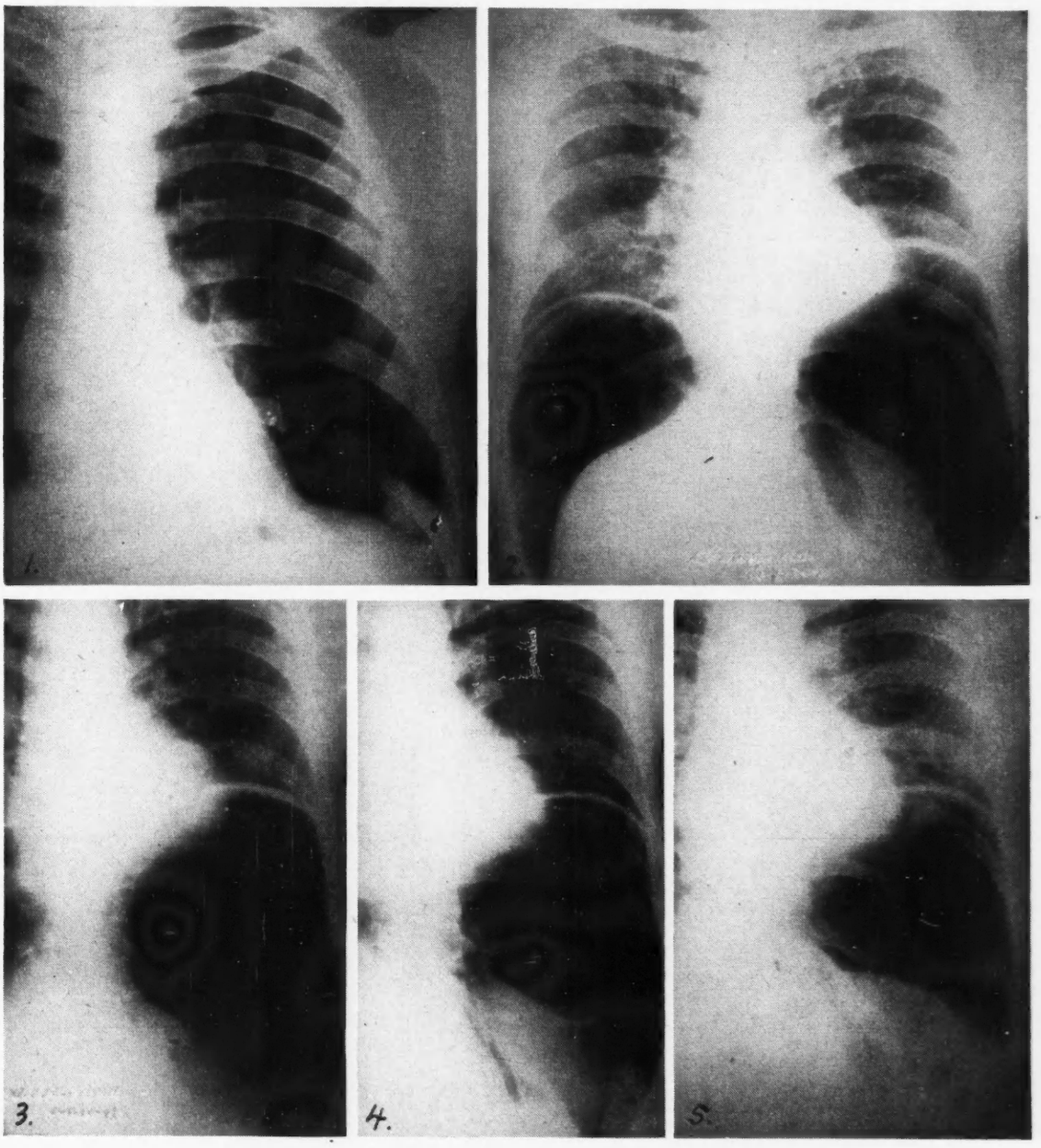

Fig. 1.—(A pneumothorax case for comparison purposes) shows a fibrin body in pleural cavity during pneumothorax therapy. **Fig. 2.** (Our case).—July 8, 1948. Pneumoperitoneum after three months of treatment. No fibrin body is seen. **Fig. 3.**—October 14, 1948. Six months after institution of pneumoperitoneum. For the first time an opaque shadow is seen in the left upper quadrant. This shadow is oval in form and measures 5½ x 3 cm. **Fig. 4.**—April 30, 1949. One year after institution of pneumoperitoneum. The oval shadow is smaller, location changed and measures 3½ x 2½ cm. **Fig. 5.**—April 13, 1950. Two years after institution of pneumoperitoneum. The shadow is still smaller in size, is now round, measuring 2 cm. in diameter and again shifted in position.

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GIANT-SIZE PARATHYROID ADENOMA

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AT THE END of the most elaborate article in the medical literature about the parathyroid adenomas and their surgical treatment, E. H. Norris, in 1947, adjured all the surgeons who, during the following ten years, would have the opportunity to operate for parathyroid adenoma to publish their observations in order to contribute to the study, still incomplete, of this severe disease.

The work of Norris included 322 cases between 1903 and 1945; since then, many other cases have been published and the total number, in the summer 1951, was of 616. If we report the present case of parathyroid adenoma, it is on account of the Norris' request and also because we believe our case is of some interest.

Mrs. A.F., age 32, came to the hospital on June 15, 1951 because, the day before, coming down off a chair on which she had stood to fix up a curtain, she had felt an acute pain in the right leg and had been, thereafter, unable to walk on that limb.

The physical examination of the right leg revealed a hard, warm and extremely painful swelling at the middle third of the tibia, anterior region. There was another swelling on the left thigh, but this one was not painful; the swelling on the right leg appeared in December 1949, and the one on the left thigh in April 1951.

We noted also a left cervical tumour, in the thyroid region, with some exophthalmos. This swelling appeared in 1935 and had grown bigger at each pregnancy; the patient was pregnant six times, and her last child was born three months ago. The pulse was 80 and the blood pressure was 115/60.

The only other detail of interest in the clinical history was that of two bouts of renal colic in the last years.

X-rays of both inferior limbs showed a large cystic lesion of the right tibia, middle third, with a transverse fracture through the lesion, and a smaller cystic lesion of the left femur, lower third. The whole skeleton was then radiographically studied and identical lesions were found on the right ulna and the left radius; the other bones, including the skull, were normal.

The hæmoglobin was 74%, the red blood count 3,780,000 and the urine was normal except for a very high excretion of triple phosphates. The basal metabolism was plus 3%.

The phosphatæmia was never determined because it was beyond the possibilities of our laboratory, but the blood calcium level, determined the next day, was 13.5 mgm. % (normal 9 to 11 mgm. %).

A diagnosis of von Recklinghausen's disease due to parathyroid adenoma was made, but, because the radiologist was of the opinion that the bony lesions might perhaps be those of a myeloma, or of a xanthoma, or metastatic lesions of a thyroid carcinoma, a biopsy of the right tibia was done on June 26, 1951. The pathological report (Dr. J. L. Bonenfant) was as follows: "The sample is formed of fibrous tissue which contains a few isolated myeloplaxes and many bony bays newly formed. The histological aspect is compatible with von Recklinghausen's osteitis fibrosa cystica generalisata."

The patient was then prepared for an operation which took place on July 6, under general anæsthesia (Dr. Frs. Cliche) by pentothal, N_2O and Flaxedil; a blood transfusion was given at the beginning of the operation.

At operation, it was our intention to remove at first the left sided tumour which we thought of thyroid origin, and then to search for the parathyroid adenoma. A long collar incision was done with a large dissection of the flaps and vertical and transverse openings of the muscles; the left thyroid lobe, at its upper extremity, was the seat of a rather large tumour half solid half cystic, but it was impossible to say if that tumour was of thyroid or parathyroid origin. It was removed very easily. The left upper region was carefully explored, and after, the lower region; in the upper region, we saw no parathyroid, but, in the lower part, a normal parathyroid was seen.

In the right lower region, in addition to a normal parathyroid, we found a growth large as a bean, dark-red in colour and rather hard, which we removed thinking it was a parathyroid adenoma. A normal parathyroid gland was seen at the upper region of the same side; the wound was then closed around two small rubber drains.

The patient stood the operation well, which lasted two hours and ten minutes, and she received 400 c.c. of blood.

The day after, the blood calcium had fallen to 10.5 mgm. %; two days later, July 9, it was 9.3 mgm., the 11th at 9.0 and the 14th at 9.0. The patient never developed tetany, but had a light sensation of numbness in the face and both hands the day after the operation. Small doses of calcium gluconate were given and this sensation disappeared completely on July 15. She left the hospital July 16, but came back periodically to have her blood calcium checked and roentgenograms of her pathological fracture taken. She was last seen on September 18; the blood calcium was 10.3, the fracture was in process of healing and her general condition was good.

Pathological report (Dr. J. L. Bonenfant) of the tissues removed at the operation:

1. The bigger tumour is a parathyroid adenoma, half cystic, half solid, 4.0 x 1.5 cm. The structure is largely trabecular, but there is occasionally a pseudo-glandular arrangement. The cells are monomorphous; the nucleus is round, hyperchromatic, occasionally irregular and large, surrounded by a pale and glandular protoplasm. The growth is very vascular. The shell is fibrous and the portion that limits the cystic area is lined by tumour cells; intra-capsular islets of identical cells are found here and there. (Parathyroid adenoma with clear cells.)
2. The smaller tumour is a vesicular thyroid adenoma measuring 10 x 5 mm.

DISCUSSION

The small tumour, that we thought to be a parathyroid adenoma, was a thyroid adenoma, whereas the large one, much to our surprise, was the parathyroid adenoma; this one weighed 65 grams. The dimensions given above are those of the pathologist; but, when the tumour reached the pathologist, at seventy miles distance, the cystic part of the growth had given way; so, the solid part only was measured.

This weight of 65 gm. is the third heaviest in the medical literature for a parathyroid adenoma; in 1939, Sharpe removed an adenoma of 120 gm., and Snell, in 1936, removed one of 101 gm. In the review by Norris, the average weight was 12.47 gm. and the adenomas were located as follows: 42.7% in the lower right para-

thyroid; 41.1% in the lower left; 9.1% in the upper right, and 7.1% in the upper left. In the present case, the adenoma was in the upper left parathyroid, consequently in the rather rare group.

According to Norris, the average duration of the disease before the diagnosis is between 5 and 7 years; here, the duration was of 16 years.

Finally, we would like to emphasize the following point: it is always possible, when one is searching for a parathyroid adenoma, to take an aberrant thyroid adenoma for a parathyroid one, as in the present case. Probably there have been cases in which another operation was necessary on account of that error. That is why, in hospitals where it is possible, the surgeon, before closing the wound, must ask the pathologist for an immediate examination in order to know if the tissues removed are of parathyroid origin; if not, the operation must be continued.

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A CASE OF GARGOYLISM*

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UP TILL NOW, only about 150 cases of gargoylism have been described in literature and the pathological findings were recorded only in a small number of cases. Because of the rarity of this condition, it was thought worth while to record yet another case of this disease, which was characterized by dwarfism, enlargement of the head, skeletal deformities, hepatosplenomegaly, sexual infantilism and mental retardation. Cirrhosis of the liver and portal congestion resulted in profuse hæmatemesis and melæna and death of the patient. Such an unusual termination of gargoylism has not been reported so far in literature. Striking cerebral changes demonstrated on post-mortem examination are also described.

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General considerations.—Skeletal abnormalities, enlargement of liver and spleen, corneal clouding and mental changes were first described by Hunter[1] in 1917 and by Hurler[2] in 1919. The grotesque appearance of these patients led Ellis Sheldon and Capon[3] to name this disease gargoylism after the quaint statues on the water spouts of mediæval Gothic cathedrals. Although in its classical form gargoylism is generally easy to diagnose, a number of cases have been described which do not conform to the typical picture of the disease. Jervis[4] who has made a study of these intermediate or formes frustes of gargoylism describes cases with gargoyle-like facies and mental deficiency, but lacking other features of the disease. However, in some of these cases, there was ballooning and vacuolation of the nerve cells of the brain, identical with the changes found in classical forms of gargoylism. Also atypical cases have been described with no corneal changes and absence of hepatosplenomegaly, and some gargoyles were found to possess a normal mentality.

Kressler and Aegerter,[5] and Ashby *et al.*[6] found vacuolated cells in organs of the body in this disease, resembling in many respects those found in certain lipoid storage diseases. Washington[7] assumed that skeletal deformities of gargoylism were due to the abnormal lipoid deposition hence naming it a lipochondrodystrophy. The same view was shared by Schmidt,[8] who concluded that lipoid storage interfered with the formation of calcified matrix at the epiphyses and also led to impaired osteoblastic activity. Lindsay *et al.*[9] suggest that swelling of the cells and their vacuole-like appearance is due to an abnormal glyco-protein deposition.

However, the assumption that gargoylism is a lipid storage disease, in common with Nieman-Pick's disease (sphingomyelin), Tay-Sach's and amaurotic familial idiocy (ganglioside) and Gaucher's disease (kerasin) cannot be entertained as long as the stored material is unknown. Extensive extractions of the dried tissue by Tanhausser[10] failed to demonstrate any changes in neutral fat, cholesterols, phospholipids, lecithin, cephalin and sphingomyelin in any organs involved in the disease. Strauss *et al.*[11] have confirmed these negative findings in their analyses. Thus, it would be premature to speak of gargoylism as a storage disease until the abnormal substance has been found.

In discussing the etiology of gargoylism,

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Jervis[4] believes it to be due to a single autosomal recessive gene, which is responsible for a defect in a single biochemical reaction. A considerable amount of evidence has now accumulated to show that single genes which are associated with specific hereditary traits control single biochemical reactions. From Jervis' study it appears that a change of an existing gene responsible for certain growth requirements might precipitate the syndrome of gargoylism.

First admission.—Miss G.L., aged 37, French-Canadian was admitted to the Hospital on December 27, 1949 because of a bout of vomiting. The vomitus had contained dark red blood clots and undigested food. She was never sick prior to her admission to the hospital. Her appetite was good, bowels and micturition regular, and she had not lost any weight. However, she has never had any menstrual periods, never experienced a sexual desire and spent most of her time at home reading comics and knitting. She has never been out to work and did only a minimum amount of housework. Born one month prematurely and weighing 8 lb. She appeared normal in every respect. When six months old, for no apparent reason, she started losing weight. At 9 months her big head was noted. When she was one year old, her mother noticed that her left hand was smaller and shorter than the right one, and since about that time her body growth was slow and the physical development retarded. She started walking at 2 years, speaking at 3, and feeding herself when 3¼ years old. She learned to read at 9, three years after going to school, which she attended from 6 years of age until she was 15. At school she was never good at anything. She never participated in any of the school games or in physical exercises. At 19 progressive shortness of vision compelled her to use spectacles and at about the same time she lost all her teeth through decay.

There was no consanguinity in patient's family. Her mother suffered from severe hypertension and some œdema few months before the patient was born. Two other sibs were premature, both born at 8 months of gestation, another sib was born at 6½ months of gestation and lived only for 2 days. This was followed by a miscarriage at 5½ months of gestation. Subsequent examination of the mother did not reveal any abnormality, except for a hypertension of 170/90; Rh testing of the mother was negative. Patient's father died in a railway accident; apparently he was very short sighted since childhood. There was no dwarfism even in the remote branches of the family traced four generations back, and none of the present members of the family appear to be in any way affected.

Examination of the patient revealed a very short, poorly developed female, height 4 feet 5 inches, span 45 inches, weight 75 lb., of a very dark complexion and deep pigmentation under both eyes. The head was large, scapho-cephalic in shape and appeared to be out of proportion to the dwarfish body, to which it was joined by a very short neck.

This unusual appearance was accentuated by a wide forehead, prominent supraorbital ridges and high cheek bones, a protuberant lower jaw, depressed nasal bridge and a complete absence of teeth. All the extremities appeared rather disproportionately short, there was some bowing of the legs, and the left forearm was found to be one inch shorter than the right, as measured from the olecranon. Gastric analysis: normal. Lumbar puncture: Queckenstedt test: normal. C.S.F.: normal.

Radiological findings.—Skull: enlarged, scaphocephalic in shape. There is a very marked thickening of the outer table. The frontal sinuses appear markedly developed, particularly to the right. The pituitary fossa is roofed in and appears to be small in proportion to the large skull. Chest: no abnormality, except for broadening and osteoporotic changes in the ribs. Arms: osteoporosis and cyst at the head of left humerus. Wrists: right wrist—the epiphyseal line is still present at the lower end of the radius and ulna. The left wrist presents an abnormality consisting in wide separation of the radius and ulna, and the ulna being somewhat longer than the radius. The same osteoporosis is noted. Flat plate of the abdomen: generalized osteoporosis of the ribs, lumbar spine and pelvis; enlargement of the hepatic and splenic shadows. Femora and knees: no abnormality, except for the osteoporotic changes. G.I. series: no significant changes.

Eventually the patient left hospital at her own request and before all examinations were completed on January 10, 1950, and on that day she was apyrexial and was feeling well.

Second admission.—She was readmitted on February 2, 1950, because of swelling of abdomen, legs and feet of two weeks' duration. Physical examination revealed free fluid in the abdominal cavity and gross œdema of the extremities. About 4 litres of fluid were removed by abdominal paracentesis. The ascitic fluid, however, reformed slowly and a fortnight after admission she had severe hæmatemesis and melæna. Despite transfusions the R.B.C. dropped from 4,300,000 on admission to 1,600,000 on February 17, with a corresponding fall in hæmoglobin. Jaundice appeared, the patient became comatose and died on February 20, 1950. A clinical diagnosis was made of gargoylism, sexual infantilism and cirrhosis of the liver.

Summary of autopsy findings.—The thoracic cavity, lung and mediastinal structures revealed no abnormality. The heart weighed 180 gm. and was small and flabby but was otherwise normal. The coronary arteries showed very slight thickening by a few scattered, raised, yellowish atheromatous plaques, but there were no areas of stenosis. The aorta was normally elastic. Its intimal surface was raised by a few longitudinally arranged yellowish fatty streaks, particularly in the abdominal aorta. The thyroid was small and weighed only 15 gm. after fixation; cut surfaces showed colloid to be present in scant amounts. One section showed a slight increase in the amount of intra-acinar fibrous tissue. The acini were small, lined by cuboidal epithelial cells, and for the most part empty; only some contained colloid. A few nests of lymphocytes were present between the acini. Two parathyroid glands were located, they were small, measuring less than 0.5 cm. in diameter, but of a normal histological appearance. The abdominal cavity contained about 3,400 c.c. of an amber coloured fluid. Aside from an enlarged liver and spleen the contained viscera appeared to be of usual size, shape and colour and were free from any gross pathological change.

The liver weighed 900 gm. and measured 21 x 18 x 6 cm. The capsule was rough and bore a rather fine nodularity throughout and was of a peculiar light orange-brown colour. Histologically the liver cells were divided into small irregular lobular masses by interlacing fine strands of fibrous tissue. The liver architecture was largely lost and liver lobules were replaced by regenerating masses of liver cords. A fine fatty droplet accumulation was seen in a few irregular zones. The gallbladder, bile ducts, and pancreas were entirely normal. The spleen weighed 350 gm. and measured 14 x 8 x 5 cm., the capsule was smooth, but near one pole there was a bluish-red nodular elevation, about 2.5 cm. in diameter, which on section was found to be a recent infarct. Histologically there was a diffuse fine increase in the amount of fibrous tissue in the pulp. The adrenals, kidneys and bladder were normal. The uterus was small measuring 3 x 2.5 x 1.5 cm. but had become converted to a thin-walled saccular structure containing greenish-yellow, purulent material. One section of the uterus showed marked atrophy, the myometrium being reduced to a thin atrophic muscle and fibrous tissue. The endometrium was represented by a single layer of epithelial cells. No gland crypts were present. A few macrophages and polymorphonuclear leukocytes clung to the lining of the uterus. The Fallopian tubes

were small and were lightly adherent to surrounding structures. Ovarian tissue was very scant in amount and difficult to locate on gross examination. Histologically no ovarian tissue could be found. Two sections from the ovarian region showed only fatty tissue containing a few para-ovarian cystic structures. The mesenteric and retroperitoneal lymph-nodes were normal. The inferior vena cava, common, external and internal iliac and vertebral veins were normal and free from thrombi. Milking of the femoral vein failed to dislodge any thrombus material.

The brain weighed 1,380 gm. Over the lateral surface of the left cerebral hemisphere, centred about the mid point of the motor gyrus, was a zone 8 x 6 cm. in which there was a dark red discoloration of the pia-arachnoid. In this zone thrombosed twig-like vessels were seen. Otherwise cerebral hemispheres, cerebellum, midbrain, pons and medulla were essentially unremarkable on external examination and on slicing, save for slight œdema of the white matter. Cortex and subcortical white matter—left precentral gyrus. The veins of the subarachnoid space were filled with fairly recent thrombus. The subarachnoid space itself was filled with a loose fibrin mesh, in which were masses of inflammatory cells. The majority were polymorphonuclear leukocytes, but mononuclears were also seen. The brain substance showed œdema and a few small blood vessels were filled with recent thrombus. Thalamus and internal capsule—left. A tiny blood vessel contained recent thrombus. Several neurons contained a yellowish-brown pigment in their cytoplasm, but showed no distension. The pituitary was normal.

Specimens of bone removed from the left humerus in the region of the anatomical neck showed some irregular thinning of cortex suggestive of small cystic formations. Bone marrow in this region was dark reddish in colour. one section of the head of the humerus showed marked rarefaction of cortex and cancellous bone. The marrow was fatty. The calvarium was thick and contained red marrow. One section of the calvarium showed condensation of cortical bone. The trabeculæ were thickened and the marrow was actively hæmopoietic.

Differential diagnosis of gargoylism. — The characteristic picture of dwarfism, skeletal deformities, corneal opacities, hepatosplenomegaly and mental retardation not found in any other disease, differentiate gargoylism from such conditions as pituitary dwarfism, hydrocephaly, cretinism, congenital syphilis, achondroplasia, cœliac disease, renal dwarfism, juvenile hepatic cirrhosis, Rh positive children born of Rh negative mothers, Albright's syndrome, and Hand-Schuller-Christian, and Gauchner's diseases. Also in the differential diagnosis of gargoylism one has to consider a very similar disease described by Morqio.[12] Morqio's disease closely resembles gargoylism in its almost identical external appearance, such as dwarfism, monstrous facies, various bony deformities, etc. However, mental symptoms, clouding of the cornea, and hepatosplenomegaly are absent in the latter. Also, the joints in Morqio's disease are supposed to be abnormally movable and there is no limitation of extension or flexion deformities as described in gargoylism. Some authorities believe the two diseases to be identical.

Of the main group of clinical and pathological changes present in our case, one may say that dwarfism, enlargement of the head, skeletal abnormalities, hepatosplenomegaly, mental retardation and sexual infantilism are compatible with a diagnosis of gargoylism or formes frustes of the disease.

The great enlargement of the frontal sinus, marked shortening of one limb, persistence of epiphysis, generalized osteoporosis and cystic changes in the bone form unusual features in this syndrome. Also extensive cirrhotic changes in the liver leading to portal hypertension, hæmatemesis and death of the patient and the striking cerebral changes have not been reported in a case of gargoylism before.

SUMMARY

A case of gargoylism is reported in which cirrhosis of the liver resulted in hæmatemesis and death of the patient. Some unusual clinical features, not described in gargoylism before, are also mentioned.

I would like to thank Professor A. Fidler, Department of Medicine, Medical School, Ottawa, for his help and encouragement in preparation of this article and also Dr. F. Norman Brown for performing the autopsy.

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CHYLOTHORAX*

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CHYLOTHORAX or chylous ascites, is not common. Goldman[1] gave a comprehensive review, and Everhart and Jacobs[2] gave a review of the literature up until 1939. Of 69 cases reviewed, trauma was responsible in 25, and in the next largest group of 22, secondary neoplasm and tuberculosis. Whiteside, Stewart and Cuthbertson,[3] Beatty,[4] Davis,[5] Shackelford and Fisher,[6] and Cellan-Jones and Murphy[7] all discussed traumatic chylothorax. Nowak and Barton[8] reported

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a case arrested by phrenicotomy, in which the etiology was not traumatic. Schaffner and Kirkpatrick[9] report successful surgical repair of the duct in a case of chylothorax due to tumour. Crassweller's case,[10] of uncertain origin, made a good recovery.

Because of the evident rarity of this condition, the following unusual case is reported.

The patient, a male, married Canadian of Irish extraction, age 63, who managed a lumber yard, was referred by his family physician and admitted to the Regina Grey Nuns' Hospital on November 8, 1949.

He gave a history of chronic, hacking cough, particularly troublesome in the winter time with occasional small amounts of mucoid or mucopurulent sputum over the past ten years. This was more troublesome in the winter of 1948-49 with more cough, sputum, wheezing and dyspnœa. However, the symptoms cleared in the late spring and he was quite well over the early summer of 1949 until late October when he developed a head and chest cold with increase in wheezing, cough, dyspnœa and sputum. To his knowledge he had never had pneumonia, pleurisy nor had he been exposed to tuberculosis. A chest x-ray taken by the Saskatchewan Anti-Tuberculosis League in May of 1949 was considered negative.

His family history was negative for chronic chest illness of any kind and there was no allergic history elicited.

He consulted his family physician one month previously who found a moderately ill man with clinical signs of fluid in the left chest. Three aspirations of approximately 600, 1,000 and 1,500 c.c. respectively were performed, on each occasion milky fluid being obtained.

On examination November 8, 1949 he appeared moderately well developed but poorly-nourished. He was comfortable in the semi-orthopnœic position but slightly audible wheezing was present and the respiratory rate was 28 per minute. The head and neck revealed slight engorgement of the superficial jugular veins when he was recumbent but otherwise were not remarkable. The chest was definitely increased in the antero-posterior diameter, appearing emphysematous. On the right side, hyper-resonance with distant breath sounds, and high pitched inspiratory and expiratory rhonchi were found. The left side revealed diminished movement of the lower two-thirds over which percussion note was flat and the breath sounds were absent. Above this level breath sounds were distant and bronchial in character. The heart appeared to be slightly displaced to the right, the sounds were distant and no murmurs were heard. The rate was 96 and regular, the blood pressure 148/90. The remainder of the examination was not remarkable. There was no clubbing of the fingers.

Chest x-ray showed the right chest to be clear, with evidence of a massive effusion on the left. Four days after admission to hospital, the patient experienced a chill with marked elevation of temperature to 104°, felt feverish and had increased cough and sputum with some pain in the right posterior chest. Clinical examination revealed crackling râles at the right base and x-ray revealed bronchopneumonia of this area. The patient was treated with intramuscular penicillin and improvement was pronounced and prompt, symptoms disappeared and the right chest cleared clinically and radiologically.

On November 18 the left chest was aspirated and approximately 1,700 c.c. of milky fluid was obtained. On direct examination this showed many lymphocytes, with rare polymorphs. and a few monocytes. It was sterile on routine culture and was negative for tuberculosis on culture and guinea pig inoculation. The protein content was 10 mgm. and the fat over 150 mgm. %.

Further laboratory work revealed a hæmoglobin of 107%, a white count of 7,100, (polys. 71, eosinophils 2, rhabs. 7, lymphs. 15). Sedimentation rate was 5 millimetres in 45 minutes. Serum proteins were 5.8 gm., albumin 3.44, globulin 2.38. Urinalysis showed a specific gravity of 1.022 and was otherwise negative. Old tuberculin was positive to 1 in 1,000 strength.

Repeat aspiration of left chest on November 21 yielded 2,600 c.c. of fluid identical with that on the first examination. At this time the patient appeared very ill, and his condition remained somewhat precarious for approximately a week, by the end of which time he began to improve. During this time he was receiving penicillin and streptomycin intramuscularly. His condition gradually improved and on December 17 bronchoscopy was performed with no abnormal findings. Serial chest x-rays revealed gradual decrease of fluid on the left side with evidence of tying-up of the left diaphragm and thickening of the pleura. A planigram series was negative.

The patient's general condition remained completely unchanged until December 23. Suddenly at 9.45 a.m. while sitting in a chair he went into collapse, became ashen, cyanotic, perspired profusely, respirations became gasping and pulse could not be obtained. He was given oxygen by nasal catheter and on examination the trachea appeared to be shifted to the right and the heart sounds were heard better to the right of the sternum, with poor to absent breath sounds over the left chest. It was felt that he had sustained a left spontaneous pneumothorax and a needle was inserted into the third left interspace in the anterior axillary line and 750 c.c. of air withdrawn. Unfortunately no apparatus for measuring pressure was immediately available but the air did appear to be under some increased pressure. This procedure was followed by some temporary improvement. A portable x-ray showed definite shift of the heart and mediastinum to the right but the left upper lung appeared to have re-expanded. The patient maintained slight improvement until approximately 4.15 p.m. when he again went into shock and died at 4.30 p.m. in spite of resuscitative measures.

Autopsy examination by Dr. N. G. B. McLetchie,* revealed the following: On opening the thorax, 1,825 c.c. of chyle was present in the left pleural cavity and the thoracic contents were correspondingly displaced to the right. An extensive dissection was performed *in situ*. The pleural membranes on the left side were perfectly smooth except at the left apex. Here there was a small, longitudinal tear 2 cm. in length on the parietal pleura, and in the corresponding part of the visceral pleura there was a small area of fine, broken adhesions. The small parietal tear led into tracks in the soft tissues and muscle of the neck, but there was no main track to admit a probe, though, on pressure, sanguinous chyle oozed out. The tissues of the left neck were removed as a single block for histological examination.

Dissection of the course of the thoracic duct *in situ* revealed no visible lymphatic system. Accordingly, transversely-cut blocks of the paravertebral region with the azygos venous system were removed for histological examination.

The left lung was collapsed, the right lung was emphysematous, and there were the usual signs of right heart failure. No other abnormality relevant to the problem of the chylous effusion was found at the autopsy; in particular, there was no evidence of tumour, venous thrombosis, or a granulomatous process.

Histological examination.—Sections of the block of tissue representing the root of the left neck revealed no abnormality in the venous system. There was a general œdema of the interstitial planes, which were opened up by a deep staining fluid containing scanty leucocytes. A thin film of recent hæmorrhage was present in some interstitial planes. The thoracic duct was collapsed, and no actual rupture was identified.

Sections of the paravertebral tissues revealed a collapsed condition of the thoracic duct and of the general lymphatic cuirasse.

Sections of the lung showed chronic bronchitis of moderate degree and general emphysema, moderate in degree and only marked in sub-pleural areas.

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COMMENT

There appears to be only one reasonable explanation for the autopsy findings. As a result of forced inspiration associated with coughing, a small emphysematous bulla must have given way, with the production of a pneumothorax. Laceration of the apical pleura and neck tissues followed, probably due to stretching and rupture of a small adhesion. The apical laceration must have torn the thoracic duct in its terminal course. As a result, chyle from the lacerated duct tracked down into the pleural cavity. The original pneumothorax was probably not large, since one might expect the pressure to have sealed the tear and allowed healing of the pleura. Evidently chyle is non-irritant to connective tissue since no sign of fibrous proliferation was found in the neck tissues.

DISCUSSION

The commonest cause of chylothorax is trauma, which usually is in the form of penetrating wounds the result of either sharp instruments or bullet injuries which destroy the continuity of the thoracic duct. In this case no history of trauma of any kind, certainly of penetrating nature, was elicited. Other causes of chylothorax are (a) secondary neoplasm (the primary site being the ovaries, stomach or bowel); (b) tuberculosis; (c) fungus infections, including yeast and moulds; (d) thrombosis of the left subclavian vein; (e) parasitic infestation, (trichina and filaria); (f) perforating lymphangitis. As far as we could ascertain, all of these etiological factors were eliminated in this case. Thus, it would appear from the evidence available that this man's chylothorax *must* have resulted from the small tear in his pleura as described in the pathological report.

SUMMARY

A discussion of chylothorax, with brief review of the literature and presentation of a case, is presented.

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SPECIAL ARTICLE

MEDICAL SERVICE SCHEMES

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AT THE PRESENT STAGE in the evolution of medical care to society, there is general agreement among responsible leaders within the profession that some type of health insurance program is essential. (Policy of the Canadian Medical Association Saskatoon, 1949). There are three types of agencies throughout the world that are attempting to provide such plans, *viz.*—government, privately owned insurance companies and most recently medical associations. Most doctors have serious objections to any government scheme. The reasons are many, well enough known to the profession generally, and require no further elaboration here.

Privately owned insurance companies have attempted to answer the need, but only in a very limited way. There are policies to cover surgery or to indemnify for specific illnesses (poliomyelitis is an example). Generally speaking, the broad field of "sickness" insurance has not been popular with the larger insurance companies. Companies will insure any event that has a definite and definable place in space—time; a shipwreck, an accident, a fire, a cyclone, death, a surgical operation, etc. These are events which lend themselves to actuarial analysis resulting in a prediction with a high degree of probability as to future occurrence. On such statistics, insurance companies can safely insure and safely expect to earn a reasonable profit. "Sickness" does not lend itself to such an analysis. Sickness may be anything, roughly from a general feeling of being unwell, real or imaginary, to an epidemic. Moreover, the costs involved in the diagnosis and care of such illness vary with each individual doctor, with the demand of the patient and with the infinite etiology of disease. Consequently, no major insurance company issues sickness insurance in such a way as to be satisfactory either to itself, the patient or the doctor. Moreover, there is the important ethical argument against a third party such as private insurance companies making a profit out of illness.

These objections in general do not apply to a plan sponsored by medical societies and such plans have grown greatly both in membership and extent, within the past five years.

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MEDICAL ASSOCIATION SPONSORED SCHEMES

There are now at least seven Medical Association sponsored medical care plans in Canada. These operate in every province except Quebec.* The original intent in sponsoring medical care plans, was to fill the growing need for some type of prepaid health insurance for the group of individuals on marginal incomes who were finding it difficult or impossible to pay doctors' fees. Below are listed some of the chief features of existing medical service schemes.

1. No income levels for subscribers; poor and rich alike are able to join at the same payable premium.
2. No direct payment is made by a subscriber to the doctor rendering the service.
3. Rigid fee schedules are set.
4. In some plans a different fee is paid to general practitioner and specialist for the same service rendered.
5. Subscriber pays the same subscription rate whether he visits general practitioner, specialist or clinic.
6. In most schemes, the doctor is forbidden to charge fees that are in excess of schedule (extra billing).

The purpose of this paper is to examine some of these conditions especially as they affect: (1) The income level of the profession. (2) The quality of practice. (3) The relationship between general practitioner, specialist and clinic practice. (4) The status of the doctor in a non-operative specialty.

RIGID FEE SCHEDULES AND THE INCOME LEVEL OF THE PROFESSION

"Lest I sound too damn noble, I wish to add that nothing helped me towards a conscientious performance so much as a conscious interest in the royalties." (Howard Lindsay, co-author and star of Broadway hit "Life with Father").

The Winnipeg Free Press, (October 3, 1950) quoted from the economist of *Saturday Night* as follows: "One of the unfortunate things about inflation is that . . . anybody who is not improving either his capital or his income in terms of dollars is actually losing heavily. All those investors who are more or less compelled to hold bonds because they are not qualified to judge the merits of different equities, or for some other reason, are doomed in such a period to suffer a serious loss. A widow who ten years ago was left an estate of $50,000 and has kept it entirely in good bonds still has $50,000, but her income even in cash has declined by reason of the fallen interest rate and its purchasing power is barely half of what it was."

The Editors of *Fortune* magazine (September, 1950) stated that the spiral of inflation was accelerating at such a rate that there was every likelihood that the purchasing power of the dollar would depreciate a further 25% within the next twelve months. The Canadian cost of living index has in fact risen from 160 in September 1950 to 184 in June 1951,[1] and is certain to rise further in the coming years.

It surely takes very little economic genius to see the impact of increasing dollar devaluation on our cost of operation, on our cost of living, and most important, on our efforts to achieve security for ourselves and our families by insurance or investment programs. What can the individual doctor do to protect himself against this progressive devaluation of the dollar in medical income?

Heretofore, the profession has been able (as have other groups in a free economy) to modify their fees in view of increasing costs of operation and of living. The profession with fairness to the community has always selectively applied this increase so that the person with the low income had very little, if any, increase in his fees; while it was the higher income groups who bore the major brunt of this rise. On the whole, this system worked well enough. No one was denied medical services, and individuals whose incomes were in the upper economic levels could afford to pay the higher rates.

There is no doubt that individuals in higher income groups demand and pay for a larger number of medical services than do those in lower income levels. Dean Clark[2] states that families with an income of less than $1,200 per year pay on the average $43 per family for medical care. The same group annually receives 1,700 physicians' house, office and clinic calls per 1,000 persons. The group with incomes at $10,000 per year and above pays $500 per year per family for medical care and receives annually 4,700 physicians' service per 1,000 persons.

With medical service schemes came fixed fee schedules for office visits, house calls, hospital calls, operative procedures, laboratory investigations, etc. Prior to the various medical plans, medical associations of the different provinces issued a schedule of minimum fees, which served as a guide to the medical practitioner. He was free, of course, to charge less than the minimum fee suggested, or he could under justifiable circumstances, charge more. It is important to emphasize that the only defence the doctor has against the effects of inflation in a free enterprise economy is this essential freedom in determining a fee. On the whole, this freedom has not been abused.

The effect of the policies of medical service schemes has been almost completely to undermine this traditional method of doctors adjusting their incomes to take care of inflationary tendencies. People in higher income groups are in increasing numbers joining medical service schemes at the same payable premium as other groups and are thereby paying, not 125 to 150% of the minimum fee, but are receiving a service at less than 100% of the minimum fee. In addition, by consistently raising rates, these services have gone beyond the reach of the "marginal" income groups, with resulting grow-

*Medical Care insurance in Quebec is available through Quebec Blue Cross and Les Services de Santé du Québec.

ing pressures from these groups to institute a Governmental "free" medical service. In short, the tendencies of medical service schemes have been to freeze medical incomes at a time when the greatest fluidity is desirable to counteract inflation. And secondly, a growing number of people in low income groups are unable to afford medical service rates. Instead of answering the demand for medical care for marginal groups, medical service schemes have seriously invaded the shrinking field of private practice, with results that, within the next three or four years, all of us will regret.

THE EFFECT OF MEDICAL SERVICE PLANS ON THE QUALITY OF MEDICAL PRACTICE

The effects are both good and bad. The low income groups of patients are assured of continuous adequate medical care which includes facilitation of diagnostic and consultation services heretofore largely denied them.

Prior to medical service schemes, however, a prominent successful doctor believing that caring for too many patients each day reduced the quality of his work or taxed his health, could raise his fees. As a consequence he would see less patients per day but he could thereby maintain his income level, his health and most important, the quality of his work. Were it necessary for the patient's welfare to spend a great deal of time with him at an office visit the doctor could do so. The charge to the patient would be for the time spent and not at a fixed rate per visit, (medical service schemes allow fixed fees per visit). We are taught in this day of the psychosomatic approach to medicine that taking time with a patient, showing him sympathy and consideration is a wonderful therapeutic tool. This requires time and where fee schedules are set per office visit such an approach is economically unsound.

There is an encouragement under existing medical schemes (with their rigid fee schedules and where fees are paid per office visit) to see more patients in a given period of time than is consistent with the practice of quality medicine. In other words, where fees are set for an office visit, a doctor has to see very many patients a day in order to have a reasonable financial return. Hence, volume of work rather than quality is encouraged.

Where no direct payment is made by the subscriber to the doctor rendering service, encouragement is given to unnecessary home and office calls, etc., which work a hardship on the doctor and further lower the quality of his work.

THE RELATIONSHIP BETWEEN GENERAL PRACTITIONER, SPECIALIST, AND CLINIC PRACTICE UNDER MEDICAL SERVICE SCHEMES

Before the advent of medical service schemes, the division of the profession into specialist and general practitioner was on the basis of training and professional recognition. Medical service schemes, however, have in some instances enforced a division based solely on a fee differential. Previously, general practitioner and specialists each could seek his own level as far as fees were concerned. Since there was no obligation on the part of authorities to make a distinction on the basis of fee returns there was more harmony in the profession.

It has been argued by some general practitioners that if subscription rates paid by the patient are the same, regardless of whom he visits, the patient might be more inclined to visit a clinic rather than an individual specialist or consult an individual specialist rather than a general practitioner.

On this tendency to arbitrarily make a difference between general practitioner and specialist, Dr. H. McPhedran[3] states, "This had a disastrous effect in Great Britain. The same could happen here and is at present shaping in that direction. Nothing is to be gained and so much will be lost by division."

THE SPECIAL EFFECTS OF MEDICAL SERVICE SCHEMES ON THE NON-OPERATIVE SPECIALISTS

In addition to the usual way of dividing specialists, one can classify them into operative and non-operative specialists. By operative specialist is meant a specialist who derives a major part of his income from operative procedures. (The general practitioner who performs a major portion of the operations in his own practice can be included in this category.) The non-operative specialist on the other hand, derives his income in the main from office consultations, *e.g.*, the internist, the pædiatrician, the dermatologist, neurologist, psychiatrist and the neuro-psychiatrist.

Emphasizing a classification such as the above is necessary under medical service schemes with their fixed fee schedules. Fees in general are set either for procedures or for office visits. The non-operative specialists rely chiefly on office visits for their income. Most of their time is spent on investigations carried out in their office. The operative specialist, as M. Sulzberger and R. Baer[4] point out, need charge little or nothing for his office visits, for these visits eventually lead to a certain percentage of operations for which he can charge the customary fees and upon which he chiefly relies for his income. The operative specialist in general need make no outlay for large office space and his necessities are usually met without expense to him at hospital laboratories and operating room.

Under existing medical schemes, the non-operative specialist is paid a fixed fee for the office visit—regardless of whether he takes an hour with a patient or five minutes. In most cases, the very nature of his practice demands that his visits be time consuming. On the other hand, an acute appendix or a hernia have few

psychosomatic components and diagnosis usually takes little time. To illustrate the point of how time consuming an office visit may be in the non-operative specialties, reference may be made to the non-operative specialty of dermatology. There is a widespread misconception that it takes only a minute to deal with a dermatologic case. Marion B. Sulzberger and Rudolf L. Baer[5] state:

"We believe that the proper examination and treatment in dermatologic cases may be, in the aggregate, more time consuming than in the average run of cases in general medical practice. Obviously, it is much easier to 'see' what is wrong with a patient's skin than what is amiss with his liver. But as a rule the patient who eventually comes to the dermatologist requires a differential diagnosis which must be based on many special examinations (bacteriologic, virus and fungus examinations and cultures, many different skin tests, examination under filtered light, serologic tests, darkfield examination, histopathologic studies, scrapings for mites, analysis of home, play and working exposures, trial diets and many adjuvant examinations and studies) in addition to detailed physical examinations and evaluation of carefully taken familial and personal histories. Regardless of whether the case is one in which diagnosis was made quickly and easily or one in which it was difficult, if topical dermatologic therapy is prescribed the manner and frequency of application, the manner of removal, the expected beneficial action and the possible by-effects of the remedy have to be gone into step by step and explained and illustrated to the patient.

Even this cursory mention of some of the routine procedures used in dermatology should convince every intelligent and unbiased person that the steps which may be necessary for adequate dermatologic diagnosis and management are likely to be more, rather than less, time-consuming than are the routine procedures used in internal medicine."

Medical service schemes favour the operative specialties further because: (a) fees set for procedures are usually high; (b) a patient who is operated on has his income curtailed or stopped. He has high hospital expenses and in addition his doctor's bill is high. The surgeon usually welcomes a scheme where the patient does not have to pay his high bill.

There is no doubt, therefore, that it is essential to have a division between the operative and non-operative specialties in the fee schedule of a medical service scheme, in order that adequate consideration be given to the nature of a non-operative specialist's practice.

This principle has been recognized in the recent fee schedule revision by the College of Physicians and Surgeons of British Columbia, and is applicable to their medical service scheme. Below is a comparison of fee schedules for office, home and hospital visits for the various groups in British Columbia (see Table I). The consultation fees in British Columbia are listed separately (see Table II). From the schedules below it can be seen that British Columbia makes a differentiation between operative and non-operative specialists.

With regard to consultation fees the following schedule (Table II) is given below.

RECOMMENDATIONS:

From all of the foregoing considerations it follows that any professionally sponsored medical-care plan should attempt to satisfy:

1. The requirements of sound economics in the presence of inflation and dollar devaluation.

2. The necessity of maintaining and improving the quality of medical care.

TABLE I.

	First calls				*Subsequent calls*			
	Office	*Hospital*	*Home*	*Night*	*Office*	*Hospital*	*Home*	*Night*
Internal medicine	$10.00	$10.00	$10.00	$10.00	$5.00	$3.00	$7.50	$10.00
Dermatology	10.00	10.00	10.00	10.00	4.00	5.00	7.50	10.00
E.E.N. and T.	5.00	3.00	7.50	10.00	3.00	3.00	5.00	10.00
General practice	5.00	3.00	6.00	7.50	3.00	3.00	4.00	7.50
Surgery	5.00	3.00	7.50	10.00	3.00	3.00	5.00	10.00
Pædiatrics	5.00	5.00	7.50	10.00	4.00	4.00	6.00	10.00
Obs. and Gyn.	5.00	3.00	7.50	10.00	3.00	3.00	5.00	10.00
Neurology and Psych.	15.00	15.00	7.50	10.00	5.00	4.00	5.00	10.00
					Neurological			

3. The desirability of a fair distribution of the total medical income among the various kinds of practitioners.

It would seem that these requirements could best be met by a recognition of three distinct economic groups within the community and by separate handling of each group.

These groups are: (1) The indigent or near indigent constituting the low income group. (2) The medium income group. (3) The high income group.

The low income group.—This group would include those who require for their general subsistence some measure of public assistance, *e.g.*, the disabled, the unemployable, the widow, the pensioner, etc. For this group there should be no hard and fast business rules to make any plan "solvent". This marginal economic group cannot possibly make any comprehensive plan solvent. Professional fees for this group should be reduced to less than the minimum fee schedule, and we should be agreed to render service to this group at a loss. We have always done so and there is no reason why we cannot continue doing so. We can then make a strong

case to Governmental agencies that our loss in the provision of essential services to this marginal group should in part be governmentally subsidized. As McPhedran[6] suggests, there should be an income level, "the state bearing in whole or in part the premiums for those persons who are adjudged to be unable to provide the premiums for themselves". (Policy of the Canadian Medical Association, Saskatoon, 1949.)

The medium income group.—For this group a reasonably solvent plan can be effected. There is now a sufficient fund of experience and statistics among the plans already in existence that a fee schedule—bearing in mind the distinction between operative and non-operative specialists

This group should provide a basis of private practice by means of which the individual doctor, specialist and non-specialist alike can have some measure of protection from the effects of rigid fee schedules on the inflationary devaluation of his income and more important still from the effects of rigid fee schedules upon the quality of his work.

SUMMARY

1. Medical care programs are reviewed.

2. The effects of rigid fee schedules are examined in the light of inflation and in the light of quality of professional work.

TABLE II.

1. Internal medicine	
(a) Formal consultation—complete history, complete physical examination, fluoroscopy if necessary, review of x-ray and laboratory findings, which may include performance of simple routine blood and urine examinations as may be necessary to confirm reported findings, with report	$25.00
2. Dermatology	
(a) Formal consultation—complete history, general physical examination and appropriate special examination	$15.00
Where biopsy is included, add	$ 5.00
(b) Minor consultation: or dealing with one particular problem	$10.00
Where biopsy is included, add	$ 5.00
3. Eye, Ear, Nose and Throat	
Consultation	$10.00
4. General practice	
Consultation	$10.00
5. Surgery	
Surgical consultation—involving one local problem	$10.00
Involving complete physical and detailed specialist examination	$15.00
6. Pædiatrics	
Formal consultation: complete history, physical examination, review of x-ray and laboratory findings, and excluding laboratory work other than routine urinalysis; including written report	$20.00
Repeat consultations: where a formal consultation for the same illness is repeated at an interval greater than thirty days, but within six months, second consultation	$10.00
7. Obstetrics and gynæcology	
Involving one local problem	$10.00
Involving complete physical and detailed specialist examination	$15.00
8. Neurology and psychiatry	
Psychiatric consultation referred or unreferred	$15.00
Neurologic consultation referred or unreferred	$15.00

—can be set up. However, there should in this group be some deterrent to abuse. "Every wage earning citizen should pay something direct to those rendering medical service in order to prevent unnecessary home and office calls, hospitalization, drugs, etc." (McPhedran).[7]

The high income group.—This third group of highest level incomes, in a free economy, has no valid claim to any place in a professionally sponsored medical scheme. For this group a doctor should have only a minimum schedule of fees to guide him, but he should be free to charge whatever he deems his services are worth (subject, of course, to the patient's right to present any grievance in this matter before a taxing committee).

3. A distinction is drawn between operative and non-operative specialists in the setting up of fee schedules.

4. Recommendations are made which may be a basis of discussion for a nation wide medical-association-sponsored health insurance plan.

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EDITORIAL

OBSCURE FEVERS

Fever of obscure origin is a challenging and provoking problem to every practitioner of experience. It calls for consideration of a great variety of diseases covering the whole field of internal medicine. Even after the most thorough clinical study, the correct diagnosis is not always achieved. Sometimes the patient recovers health without benefit of diagnosis. Usually, however, the true nature of the cause is established. This is done at times by eliciting a previously neglected point in the patient's history, or by discovery of a new physical finding. More often, however, diagnosis is achieved by use of appropriate laboratory tests, by following the natural course of the disease, or by the response to a therapeutic procedure.

In general, obscure fevers of short duration, even though met more frequently, are not too puzzling. Most of them obviously are acute infections, the majority probably of viral origin. The clinical characteristics and diagnostic methods are far better known for bacterial than for viral infections. It is usually not practical to do animal inoculations in order to prove or exclude pathogenic viruses. Furthermore, many of the known pathogenic viruses are not pathogenic to the common laboratory animals. As an example, measles may not have been recognizable as a distinct disease except for the associated characteristic skin eruption.

Greater diagnostic emphasis should be placed on febrile diseases of long duration. These can be usefully grouped according to height of the fever. A higher temperature may well entail a more serious prognosis. Prolonged low-grade fevers (around 100° F.) may occasionally be the first indications of serious illness. On the other hand, they may persist for years without any objective manifestations of disease. Thus Reimann has designated a particular form of this as habitual hyperthermia. He applies this term to patients, usually women between the ages of 20 and 50, who exhibit over a period of years frequent temperature elevations up to 100.5° F. with vague complaints of fatigue, insomnia and malaise. When no evidence of organic disease is established after careful study and a suitable period of observation, the patients should be persuaded to disregard the fevers and make the best possible adjustments to the other symptoms.

One should not overemphasize low-grade fevers in children, especially those under 2 years of age. The temperature regulating mechanisms are not fully developed in early life and it is therefore rather common to have moderate temperature rises after exercise or even emotional upsets.

A.H.N.

CHEMOTHERAPY

Early development of chemotherapy was concerned chiefly with treatment of tropical diseases. Considerable progress has been made, but further advances are still needed. Chemotherapy of malaria occupied a large proportion of the total effort for many years. This has now reached a reasonably satisfactory basis, largely as a result of work done during the war. More attention is being given today to the diseases for which no adequate chemotherapy exists, or for which new and promising drugs have been produced, but require further study. Drugs of considerable promise in the treatment of amœbic dysentery, schistosomiasis and filariasis have been developed, and studied extensively both clinically and experimentally. The latter two diseases are due to parasitic worms which occur widely in tropical and subtropical areas and are the cause of much ill health.

Probably the most important advance in chemotherapy has been the discovery of the antibiotics, many of them having a useful range of activity against pathogenic bacteria. The latest among these are chloromycetin, aureomycin and terramycin, all produced by moulds. Chloromycetin has been identified chemically and synthesized. These new antibiotics have extended the range of bacterial infections that can be treated with good effect to include brucellosis, typhoid fever and perhaps whooping cough. Furthermore they are of particular interest since in addition to

being effective against pathogenic bacteria they are also effective against rickettsial diseases such as typhus and scrub typhus fevers and even against some virus infections. Rickettsiæ and viruses must resemble in their requirements very closely the host cells. It is, therefore, quite surprising to find that there are chemical compounds which can destroy the infective agent while having little or no ill effect on the infected host. They have therefore opened up a new field of chemotherapy.

The other main advance in bacterial chemotherapy has been in the treatment of tuberculosis. Carefully conducted studies have established the value as well as the limitations of streptomycin in the treatment of the various forms of tuberculosis infection.

Chemotherapeutic research extends far beyond synthesis of new drugs, discovery of new antibiotics, or even the experimental study of infections. We must understand the actual mode of action of a drug on the micro-organism under attack in order to secure a rational basis for future development. To learn about the action of a drug, we must first have as complete a picture as possible of the normal processes of life of the micro-organism. Then we can study the changes produced by the drug with some hope of deducing what changes in its chemical structure would make it a more effective chemotherapeutic agent.

It is from work of this kind that we may hope to learn eventually how to overcome the phenomenon of drug resistance. This phenomenon, *i.e.*, emergence under treatment of a strain of infecting organisms with greatly enhanced resistance to the drug, occurs in varying degree with different chemotherapeutic agents. With penicillin it is rare, however, with streptomycin it is so frequent as to be a serious obstacle to effective use of the agent. Unfortunately, it is true that a new chemotherapeutic drug, however great its initial promise, may in a relatively short time have lost a great deal of its value owing to development of drug-resistant strains. It seems clearly indicated that every attempt should be made to solve this problem. A.H.N.

Editorial Comments

TWO NEW JOURNALS

We wish to welcome to the rapidly increasing medical journalistic fold two new journals which started publication in January of this year. *Diabetes*, published by the American Diabetic Association, will provide an official Journal for the Association and furnish the medical profession with information concerning diabetes and related fields of medicine. This is edited by Dr. Frank N. Allan and will appear every other month.

Metabolism: Clinical and Experimental, edited by Dr. Samuel Soskin and published once a month by Grune and Stratton, Inc., it is hoped will assist in giving expression to the remarkable expanding science of metabolism. The physician should find this of help in keeping abreast of many applications to clinical practice, affecting diagnosis, prognosis and therapy in almost every branch of medicine.

GERIATRICS AND PÆDIATRICS

During the early months of life infants are entirely dependent on their environment for the gratification of their needs, physical, emotional, and to a large extent, motor. This is equally true for the debilitated geriatric patient. The practice in the past has been to quote dosages of drugs for adults and sometimes to annotate the pædiatric doses; now with an increasing number of the population in the geriatric range this dosage will have to be considered. In the use of drugs such as morphine and the barbiturates fractions of the adult doses are used for children and the aged. In many young and old persons barbiturates induce excitement rather than sleep. Chloral hydrate and the bromides are excellent soporifics for pædiatric and geriatric patients, and at present do not have as much use in the middle age groups. Hydration therapy must be very carefully controlled in the aged and young as there is the great danger of pulmonary œdema. Similarly in the matter of diet the infant and child are gradually introduced to adult foods. Geriatric patients revert to softer foods with less fat as dental and gastro-intestinal difficulties arise. Pablum is now used with equal frequency in young children and edentulous old people, both of whom need soft food with a high protein content and vitamins. Both ends of the life span are more susceptible to changes in climate and weather with ensuing headcolds and the sequelæ therefrom; both age groups are equally prone to traumatic accidents. In the five to fifteen year group accidents are a primary cause of death, fractures in this age group may be greenstick or torus (early) or complete (later), while in the aged person accidents, usually falling, give rise to complete fractures of the partially atrophic bone, and complications, such as orthostatic pneumonia or vascular thrombosis cause many fatalities. The nervous stability of the young and aged is influenced by environmental and social changes and appropriate treatment is the same in both.

The physician must always consider bed rest as a highly unphysiologic and definitely hazard-

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ous form of treatment to be ordered only for specific indications and discontinued as early as possible with the very young and very old.

There is more truth than fiction in the statement, "He is in his second childhood". J.A.S.D.

GOING TO THE UNITED KINGDOM?

Through the medium of a B.M.A.-C.M.A. exchange of currency, three British doctors were able to finance visits to Canada during the year 1951. We are grateful to the Canadian doctors who made this arrangement possible by depositing dollars with us and receiving from the British Medical Association an equivalent sum in sterling on arrival in the United Kingdom.

This plan, which has the approval of the Bank of England, will again operate this year and it is hoped that Canadian doctors contemplating travel in Britain will assist by notifying the General Secretary of their willingness to participate.

Assuming an exchange rate of $2.80 per £, the Canadian Medical Association will be glad to receive sums up to $560 and to arrange with the B.M.A. to pay the equivalent up to £200. Conversely, the Canadian Medical Association will provide up to $560 to two British doctors who will visit this country.

Although you as a Canadian traveller will not find it difficult to obtain the sterling currency you require, our British colleagues are not so fortunate. Members desiring to participate in this excellent plan are requested to communicate with the General Secretary, 135 St. Clair Avenue West, Toronto 5, several weeks in advance of departure to permit all details to be transmitted to the British Medical Association.

VACCINATIONS FOR INTERNATIONAL TRAVEL

The World Health Organization has issued a list of vaccinations required at present in 132 countries and territories from travellers crossing international borders by land, sea or air. The vaccinations most generally required are against smallpox, yellow fever and cholera. Several countries also specify inoculation against typhoid and paratyphoid fevers, typhus, diphtheria and tetanus.

The requirements specified in the new WHO listing follow the 1944 International Sanitary Regulations which, for a majority of the countries named, are being applied for the last year. On October 1, 1952 the new International Sanitary Regulations adopted by the Fourth World Health Assembly (1951) will replace the existing international conventions. Vaccination certificates issued under existing conventions will continue to be recognized by all states which have accepted them until now, including those states which have already adopted the new International Sanitary Regulations.

PANIC AND PUBLIC RELATIONS

Probably nothing can make an impression—good or bad—on a patient more quickly than whether or not he is able to get a doctor in an emergency. The problem is complicated because it seems that emergencies almost never occur during office hours and are most frequent between midnight and six a.m. Also there is usually a marked divergence of opinion between the patient and the doctor as to what constitutes an emergency.

Nevertheless the panic of a patient over an emergency—real or supposed—has a bearing on his attitude towards the profession out of all proportion. It takes few stories, circulating by the press and word of mouth and picking up refinements as they go, to earn for the profession a reputation of callousness which the record shows is not entirely deserved.

It may be said that the solution lies in tightening up the doctor's method of having his calls attended to when he cannot. Some doctors say "I haven't had any complaints from my patients." But the trouble is that a large proportion of the Canadian population have no regular family physician. In the United States it has been said that only one person in every three has a family doctor. Whether or not that person is attended to in emergencies is problem enough. But what about the other two?

The profession's answer to this problem in service and public relations is the emergency call system. It has three obvious objectives. To see that: (1) a doctor will always be available; (2) the emergency call load will be evenly distributed; (3) the public will always know how to get a doctor in a hurry.

Emergency call systems are by no means new and have been operating in various forms in Canada and the United States for many years. Recently the American Medical Association conducted a study of the emergency call programs of 143 counties in 38 states. In reviewing the findings the A.M.A. points out the dangers of over-generalizing on objectives, needs and methods. However some conclusions can be drawn.

Probably the most obvious fact is that the larger the population of an area served by a society, the more necessary is a formal system of handling emergency calls. In thinly populated areas, the few doctors can arrange among them-

selves some system. Indeed they must if a doctor's services are to be available at all times. In more populous areas, where the need is obvious, the A.M.A. found that emergency call systems are operated in three ways: (1) hospitals; (2) privately owned physicians' telephone service; (3) society-operated. In smaller counties, where most of the doctors are on the staff of one hospital, the hospital switchboard and a roster of duty physicians is found satisfactory.

In more heavily populated counties, there are more hospitals and it is unusual for any one hospital to have most of the doctors on its staff. Under these circumstances, the A.M.A. points out, "it is more satisfactory to find some non-hospital switchboard through which calls can be routed to all the doctors serving the emergency program. In some of these counties, the problem is solved by the use of the telephone exchange operated by the medical society; in the majority of cases, however, the society makes use of an established private exchange which handles emergency calls by means of a roster provided by the society."

Few people in a community are busier than the doctor. Allocating emergency calls is one of the chief problems. In smaller counties studied by the A.M.A. a straight rotation system is used with one or more doctors taking all emergency calls during a fixed period of time. In larger counties the areas are subdivided and the doctor on duty takes emergency calls only in his area, saving considerable time and gasoline in the process.

The report shows that the smaller county rosters tend to include all doctors except those excused by age or disability. Larger counties can usually find enough volunteers to see that enough physicians are always available to handle calls.

The report which outlines the operating method of each of the plans, is too long to reproduce in these columns. However some aspects, viewed in the light of existing circumstances in Canada, are worthy of consideration.

It is not enough to set up an emergency call system, and then expect it to make itself known to the public. If it is to serve the people in a time of need, and is to earn goodwill for the profession, it must be promoted. Many societies in the United States carry out an inexpensive but effective advertising campaign in the newspapers and radio stations. Advertisements are along the lines of "If you need a doctor in an emergency, day or night, telephone ....." In some cases doctors attach small stickers carrying the emergency number on to bills and correspondence. In most cases cards carrying the telephone number are distributed to hospitals, police and fire departments, hotels, taxicab companies, ambulance services, civic offices, newspapers and radio stations. Telephone operators are acquainted with the number which is often placed at the front of the telephone directory. Printers producing telephone number cards for advertisers are asked to carry the number along with those of the police and fire departments. In many communities, merchants sponsor "welcome wagons" to acquaint new residents with community services and the merchandise of local stores. In many cases the emergency call number card is inserted in give-away literature.

The A.M.A.'s report indicates that there can be no master plan to be applied willy-nilly. In each community there are local conditions and circumstances which must be taken into account. But the need is there and the profession has shown an awareness befitting its responsibilities. Many areas across Canada need such a service. The experience of those in both Canada and the United States who have pioneered is available to all members of the Canadian Medical Association, which invites enquiries. The C.M.A. would also be interested in learning of the experience of groups of the profession in Canada which have implemented emergency call programs.

Although experience shows there is no fixed formula for emergencies, the program of the Chittenden County Medical Society of Vermont is reproduced here as representative of those for areas of comparable population. County population: 52,098; largest city: Burlington, 27,700. Society members, 110.

The Chittenden County emergency medical plan covers only the city of Burlington and the adjacent city of Winooski. The county medical society leases a line to the switchboard of a commercial telephone answering bureau in Burlington for $15.00 a month. For an additional fee, the bureau operates the plan. The society supplies the bureau with a list of physicians who will answer emergency calls.

Since Burlington has a modest medical centre, it has a number of specialists who have not the equipment to care for emergency house calls. Feeling that this work is, in general, the obligation of the younger men, the society decided that men who have attained the rank of attending physician in a hospital and men who have been in practice over ten years should be excused from the plan; most of the remaining members of the society are willing to take calls in rotation.

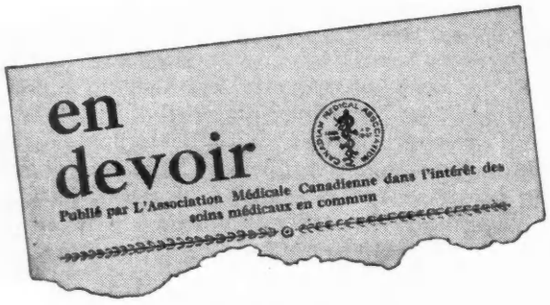
The telephone number of the Bureau has been publicized in local newspapers on several occasions; it is known to the telephone company, which often itself receives emergency calls. The number is listed in the telephone directory in a way which the society believes makes it convenient to the public in time of need.

The public has used the service heavily from its beginning and has now settled down to a steady rate of about 75 calls per month, in a community of forty thousand. Only about 5 to 10% of the calls are not emergencies and many of these could not safely have been so classified without examination by a physician.

Each society member in the two towns is taxed three dollars a year towards the cost of the

plan. This is almost adequate to cover the expense of operating the system, which comes to about thirty dollars a month.

A few physicians abuse the service by referring to it undesirable calls which they would be able to take themselves. In general, however, the service meets satisfactorily the needs of the community.



PANIQUE ET RELATIONS PUBLIQUES

Aucune autre situation, semble-t-il, peut créer plus rapidement une impression—bonne ou mauvaise—chez un patient, que la possibilité d'obtenir ou non un médecin, dans un cas d'urgence. Ce problème est compliqué d'ailleurs car il semble que les cas d'urgence ne surviennent presque jamais pendant les heures de bureau et sont plus fréquents entre minuit et six heures du matin. De plus, il existe généralement une conception différente marqée entre le patient et le médecin au sujet de ce qui constitue un cas d'urgence.

De toute façon, la panique d'un patient à l'égard d'un cas d'urgence—réel ou imaginaire—possède une répercussion extraordinaire sur son attitude à l'égard de la profession. Il suffit de quelques faits, révélés par la presse, transmis de bouche en bouche et exagérés au fur et à mesure, pour jeter du discrédit sur la réputation médicale, qui pourtant a prouvé dans le passé qu'elle ne mérite pas une telle injustice.

L'on peut dire que ce problème pourrait être résolu en établissant des règlements plus sévères pour les médecins, qui consisteraient à faire nommer un remplaçant pour le médecin qui ne peut répondre à ses appels. Quelques médécins disent: "Je n'ai pas eu de plaintes de mes patients". Mais le problème se complique par le fait qu'une grande partie de la population canadienne ne possède pas son médecin de famille. Aux Etats-Unis, l'on rapporte même qu'une personne sur trois possède son médecin de famille. Savoir si cette personne obtient son médecin en cas d'urgence est déjà un problème, alors qu'arrive-t-il dans le cas des deux autres?

La réponse offerte à ce probléme par la profession elle-même, ce qui aidera au service et aux relations publiques, consiste dans un système pour répondre aux cas d'urgence. Il s'agit d'un triple objectif: (1) Un médecin sera toujours disponible; (2) le nombre des appels d'urgence sera partagé plus également; (3) le public saura toujours comment obtenir un médecin pour un cas urgent.

Un système pour répondre aux cas d'urgence n'est pas une nouveauté et fonctionne depuis plusieurs années dans beacoup d'endroits sous différentes formes, au Canada et aux Etats-Unis. Récemment l'Association Médicale Américaine a poursuivi une étude concernant les programme pour les cas d'urgence dans 143 comtés et 38 états. En révélant les résultats l'A.M.A. fait remarquer les dangers de trop généraliser les buts à atteindre, les besoins et les méthodes d'agir. Cependant, quelques conclusions peuvent être tirées.

L'un des points les plus évidents démontre que dans les endroits où la population est plus considérable et desservie par une société, il est plus nécessaire d'avoir un système définitif pour prendre soin des appels d'urgence. Dans les endroits où la population n'est pas nombreuse, les quelques médecins peuvent s'arranger entre eux pour établir un système adéquat. D'ailleurs, ils doivent agir ainsi pour que les services du médecin soient disponibles en tout temps. Dans les grandes villes, où le besoin est évident, l'A.M.A. a constaté que le système des appels en cas d'urgence était réparti selon les trois façons suivantes: (1) hôpitaux; (2) les services téléphoniques organisés par les médecins eux-mêmes; (3) les systèmes fonctionnant au sein de la société.

Dans les comtés moins populeux où la plupart des médecins font partie du personnel d'un hôpital, ceux-ci sont en devoir à tour de rôle et sont avertis par un système téléphonique de l'hôpital, dans les cas d'urgence. Cette façon de procéder s'est avérée satisfaisante.

Dans les comtés plus populeux, il existe plus d'hôpitaux et il est rare que l'une ou l'autre de ces institutions compte tous les médecins de l'endroit parmi leur personnel. Dans de telles circonstances, l'A.M.A. fait remarquer: "Il est plus satisfaisant dans ces cas, d'avoir un système téléphonique en dehors de l'hôpital, qui puisse placer les appels à tous les médecins servant dans les cas d'urgence. Dans quelques-uns de ces comtés le problème est résolu par un échange téléphonique sous la juridiction de la société médicale; dans la majorité de ces cas cependant, la société emploie un échange téléphonique privé, qui s'occupe de tous les appels d'urgence en les partageant à des médecins déterminés, dont la liste est fournie par la société.

Peu de personnes dans une ville sont plus occupés que les médecins, alors il existe un autre problème dans le partage des appels d'urgence. Dans certains comtés moins populeux où l'A.M.A. a poursuivi une enquête, un système de partage à tour de rôle pour un ou plusieurs

médecins qui s'occupent de tous les appels d'urgence au cours d'une période déterminée, a été établi. Dans les comtés plus considérables, le champ d'action est divisé en plusieurs régions et le médecin en devoir s'occupe seulement des cas d'urgence dans la section à laquelle il a été assigné, ce qui épargne beaucoup de temps et d'essence.

Le rapport indique que la liste des médecins ainsi nommés inclut tous les médecins excepté ceux qui sont excusés par l'âge ou l'infirmité. Quant aux comtés plus considérables, il existe généralement un nombre suffisant de médecins volontaires disponibles pour que tous les appels d'urgence soient répondus.

Le rapport qui décrit la façon de procéder de chacun de ces systèmes serait trop long à reproduire ici. Cependant, quelques aspects considérés en relation avec les circonstances qui existent au Canada méritent notre considération.

Il n'est pas suffisant d'organiser un système pour répondre aux appels d'urgence et de croire qu'il se fera connaître par lui-même parmi le public. S'il doit servir la population dans les cas d'urgence et en même temps rehausser l'admiration envers les médecins, ce système doit être annoncé. Plusieurs sociétés aux Etats-Unis publient dans les journaux et à la radio, des annonces peu dispendieuses mais efficaces. Ces annonces diront par exeple: "Si vous avez besoin d'un médecin dans un cas d'urgence, soit la nuit ou le jour, téléphoner ....." Dans certains cas, les médecins envoient avec leurs lettres ou leurs comptes, une petite carte indiquant le numéro à signaler en cas d'urgence. Dans la plupart des cas, ces cartes, indiquant le numéro de téléphone, sont distribuées aux hôpitaux, aux services des incendies et de la police, aux hôtels, aux compagnies de taxi, aux services d'ambulance, aux bureaux civiques, aux journaux et aux postes radiophoniques. Les téléphonistes connaissent le numéro à signaler en cas d'urgence, car ce numéro est souvent placé au début, sur une page spéciale du bottin. Les imprimeurs, qui distribuent des cartes pour les annonceurs sont priés d'imprimer le numéro pour les appels en cas d'urgence, comme ils le font pour les services de la police et des pompiers. Dans plusieurs villes, les marchands commanditent des annonces de bienvenue pour les nouveaux arrivés et dans plusieurs cas, le numéro de téléphone à signaler en cas d'urgence est indiqué sur les annonces que l'épicier distribue.

Le rapport de l'A.M.A. indique qu'il n'existe pas de plan général qui puisse être adopté à ce sujet, car chaque endroit est soumis à des conditions et des circonstances spéciales. Tout de même le besoin est là et la profession a montré un intérêt qui est digne de ses responsabilités. Plusieurs régions au Canada ont besoin d'un tel service. L'expérience de ceux qui ont établi les premiers pas dans ce domaine, au Canada comme aux Etats-Unis, est à la disposition de tous les membres de l'Association Médicale Canadienne, qui invite toute demands relative à ce sujet.

L'A.M.C. serait intéressée aussi à connaître les résultats obtenus des groupes professionnels au Canada, qui ont établi un système pour répondre aux appels d'urgence.

Bien que l'expérience démontre qu'on ne peut adopter de formule fixe pour les cas d'urgence, le programme de la Société Médicale du comté de Chittenden dans le Vermont, offre un programme assez représentatif pour les régions possédant à peu près la même population. Population du comté, 52,098; plus grande ville, Burlington, 27,700. Membre de la Société, 110.

Le plan médical pour les cas d'urgence dans le comté de Chittenden couvre seulement la ville de Burlington et sa ville voisine, Wincoski. Dans ce comté, la société loue au prix de $15.00 par mois, une ligne téléphonique à Burlington dans un bureau qui s'occupe de répondre aux appels téléphoniques. Pour des frais supplémentaires, le société médicale s'occupe de ce programme et fournit au bureau de la centrale téléphonique, une liste de médecins qui pourront répondre aux appels d'urgence.

Comme Burlington possède un centre médical modeste, elle possède un nombre de spécialistes qui n'ont pas le nécessaire pour répondre aux appels d'urgence à la maison. Comme il a été pensé que ce travail en général revient aux plus jeunes médecins, la société décida d'exempter les médecins résidents d'un hôpital ou ceux qui pratiquent la médecine depuis plus de dix années; ainsi la plupart des membres qui restent dans la société consentent à répondre aux appels à tour de rôle.

Le numéro de téléphone du bureau a été publié plusieurs fois dans les journaux locaux, et la compagnie de téléphone transmet elle-même ce renseignement à ceux qui téléphonent pour un cas d'urgence. De plus, le bottin du téléphone contient aussi ce numéro d'une telle façon qu'il peut être facilement trouvé par ceux qui en ont besoin.

Le public a beaucoup employé ce service depuis son établissement et il existe actuellement un flot régulier de 75 appels par mois parmi une population de quarante mille âmes. Seulement une proportion de cinq à dix pour cent des appels ne sont pas des cas d'urgence, et plusieurs de ceux-là ne pouvaient être déclarés comme tels sans un examen du médecin.

Chaque membre de la société dans ces deux villes, paye des frais de trois dollars par anneé pour subvenir aux dépenses de ce système. Ce montant est adéquat pour le coût d'opération qui se chiffre a trente dollars par mois environ.

Une minorité de médecins abusent de ce service en y transmettant les appels indésirables qu'ils pourraient eux-mêmes répondre. Mais en général, ce service a répondu avec beaucoup de satisfaction aux besoins de la communauté.

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MEN AND BOOKS

DR. JOHN BROWN OF EDINBURGH*

F. ARNOLD CLARKSON, M.B., *Toronto*

IN THE BROWN FAMILY there were five John's in succession. The great-grandfather, a shepherd boy on the braes of Abernethy, taught himself Greek and much else, and was so precocious that his certificate of church membership was withheld, because there was "suspicion that he had acquired his learning through a compact with the devil". His great-grandson remarked, "That astute personage, Auld Clutie, would not have employed him on the Greek Testament". But he fought his way into the ministry to become Professor of Theology in the United Presbyterian Church. The grandfather and the father of our John Brown were also ministers. The latter was stationed at Biggar where, in the Secession Manse, his second child was born on September 1810, and named John.

Biggar is a small stone town in Lanark, forty miles south of Edinburgh. Its charter dates from the 14th century, and in 1720 a medical school was founded, where for about seventy-five years, young men were apprenticed to the town doctors, some of whom were of national reputation. The citizens were justly proud of their town, because here William Wallace defeated Edward the First, and the little burn, the "Red Stye", ran blood for days. They recorded their pride and vanity in a saying "London's big but Biggar's Biggar".

At the Manse, surrounded with deep parental affection, the little boy acquired a love of books from his father's well-stocked library. His mother died when he was quite young so he was brought up by his kindly grandmother, and his father taught him the rudiments of Latin and mathematics. Then came his father's call to a church in Edinburgh (1821) and John was sent to a Latin school, where his little shirt-tailed coat caused some banter from the city boys who wore round jackets. But John had plenty of spirit and was quite able to hold his own in the fights behind the school, just as, some years later, Tom Brown thrashed Bully Flashman. When he entered the High School he seemed to have been a general favourite and was second dux in a class of one hundred. He read the *Iliad* and the *Odyssey* for private study.

Although the three other John Brown's had chosen the Church, young John seemed to have early set his heart on Medicine. After one year in the Arts course, he registered in the medical school and was apprenticed to Mr. Syme for six years. His preceptor was then just reaching his prime and was more than locally famous for the rapidity of his operations, which in the days before anæsthesia, was of great importance. Brown could not have found a better teacher in all Scotland. Of him it was said that he never wasted a drop of blood, or a drop of ink. His patients called him "the doctor who ran when he walked". Once, as Syme's surgical clerk, John received James, the Howgate carrier, as he lifted down Allie, at the gate of Minto House Hospital—names never to be forgotten by readers of *Rab and his Friends*. Syme discovered, in one of his many researches, a method of applying rubber to cloth and rendering it waterproof, but did not patent his discovery. Another Scot, however, was sharp enough to do so, and the name McIntosh is now more widely known than that of Syme.

In 1833 he received his degree from Edinburgh University and immediately hung out his shingle in that city. When Brown began to practice in Edinburgh dirt and disease were the big sacraments. The fetid "Wynds" with their offensive smells, or the "Closes", like Big Lochend's at the top of an outdoor stairway of ninety-six steps, with all the disadvantages of sorrow and extreme poverty, were an everyday adventure for doctors. The midwifery of the Cowgate and the Cannongate has been described by one of our Canadian students at that time as "without fire and without water".

Many of the people on the street were pockmarked from smallpox, for Jenner's unscarred throng had not yet arrived. Inoculation was still used. Typhus and typhoid, because both were accompanied by a rash, were not differentiated till 1828. They were much too common and took a great toll of young people. But the "Captain of all of these men of death" was tuberculosis and was so to remain for the better part of a century.

One of the most common conditions Scottish physicians had to contend with was delirium tremens. Even with the large quantity of alcohol we are now consuming, it is amazing to read that in the beginning of the nineteenth century every fourth building in Glasgow was a public house and fifteen thousand people got drunk every Saturday night. Temperance was so uncommon that it was suspect. An insurance company is said to have refused a policy to a man who declared he was a teetotaller. These were the days when the poor found happiness only in the bottle and peace only in the grave. The shocking sanitation was responsible for the foul water supply. The conditions in the operating room were revolting, and surgeons took pride in the disgusting state of their raiment. In the squalor of the mines, women, "chained, belted and harnessed", worked stripped to the waist. Children went into the mines at the age of five. Wagon-loads of children were sent from the workhouse to the mills. Young boys climbed up the chimney flues and had salt rubbed into their bleeding knees when they descended.

But of this economic turmoil which stormed overhead, we have hardly a word in all Brown's

*Part of a paper read before the Medical Historical Club, Toronto.

voluminous writing. Jane Austen wrote her novels in the midst of Napoleonic wars, and yet gave not a hint of that world-shaking event; and Sir Thomas Browne never referred to the great cataclysm of his day.

The patronymic "Brown" is found in most European countries. Next to "Smith" it is the most common name in Ontario. The Browns have played an important part in the history of English speaking countries, in every walk of life. But John Brown was almost alone among the many other doctor-authors in carrying on a large general practice to the end of his life and at the same time contributing so many essays, criticisms, translations and lectures that it is hard to understand where he found the time.

He was a most voluminous letter writer over a period of years, beginning when he first left home. These family letters were often humorous and always affectionate. When he was in Chatham, as Dr. Scott's assistant, he sent a list of his expenses to his sister, who seemed to feel she must keep a check on his extravagances. From the list submitted, one might feel that there was some measure of inflation at the time (1841). A bottle of soda water cost 1/6, "steward 2/6, ginger beer 2/, clogs like my father's 10/6, pair boots £1.8, quarterly collection at Ebenezer Chapel 2/, to a woman 2/, Whately's *Logic* (it is a good book, but in my circumstances I should not have bought it) 12/, subscription to the Temperance Society 3/6. I have missed out the washings, about 14/4, perhaps a little more; not one of the stockings has a single hole". He writes long letters to his brother William, giving him fatherly advice on his proper conduct in religion and many other personal matters, although there was a difference of only a year or so in their ages. William's letters in reply seem to show that he didn't take kindly to such patronizing. Many of these epistles refer to his dogs, all of which had charming characteristics and were always a part of his household.

His letters to his father give details of his day's work at Chatham. "Up at half past seven and put laboratory in order. At eight prayers read by the doctor (a Scot), then breakfast with beefsteaks. Post books for one hour. Out in the gig with the Doctor where typhus is very prevalent", and so on through a general practitioner's day, winding up at nine with supper of porridge, bread and cheese, no sugar; no bath. When he had a cold the Doctor ordered a hare's skin for his breast and a pair of clogs. With night comes sleep, and he "immediately returns home" and is low-spirited. Although he had little time for reading, he managed about eighteen or twenty verses of the Greek Testament, and a bit of Butler every night.

His preceptor's income was £1,200 a year. Brown helped the total by bleeding at 2/6, teeth 2/ each, visits to patients 5 to 7/. The Doctor sent out £4.5 worth of medicine a day, which young Brown dispensed. He was so busy, answering the door and rubbing down the patients who came from the vapor baths, that he had no time to examine the flowers of the neighbourhood. But he found the chicory, (Blue Sailor) as plentiful in Kent then as it has now become on our own roadsides.

In June 1832, the Doctor was away and Brown was in full charge.

> "I took off a young man's arm in the morning and found the operation ridiculously easy. The whole of the stump with the exception of the corner where the ligatures hung out, healed *prima intentione*. The poor woman whose breast I removed, is quite well. . . . We have cholera raging on one of the convict ships—ninety cases and about thirty deaths. I will thank you in your letter to give me the latest information about the transfusion plan, specifying the quantities of salt and whether or not it promises much. I shall certainly try it and perhaps also the actual cautery along the spine, after a certain time that is, when the collapse has fairly set in. I have little faith in anything and am almost sure that all the cases have been overtreated in this stage."

Two weeks later the cholera spread to the town, with thirty cases and ten deaths. The people showed great confidence in the two cholera doctors who were busy night and day. Some time later he wrote:

> "I shall never forget a proof I myself got twenty years ago, how serious a thing it is to be a doctor, and how terribly in earnest people are when they want him. It was when cholera first came here in 1832 I was in England at Chatham, which you all know is a great place for ships and sailors. This fell disease comes on generally in the night; as the Bible says 'it walks in darkness', and many a morning I was roused at two o'clock to go and see its sudden victims, for then is its hour and power.
>
> "One morning a sailor came to say that I must go three miles down the river to a village where it had broken out with great fury. Off I set. We rowed in silence down the dark river, passing the huge hulks, and hearing the restless convicts turning in their chains on their beds. The men rowed with all their might; they had too many dying or dead at home to have the heart to speak to me. We got near the place; it was very dark, but I saw a crowd of men and women on the shore, at the landing-place. They were all shouting for the doctor; the shrill cries of the women, and the deep voices of the men coming across the water to me. We were near the shore, when I saw a big, old man, his hat off, his hair gray, his head bald; he said nothing, but turning them all off with his arm, he plunged into the sea, and before I knew where he was, he held me in his arms. I was helpless as an infant. He waded out with me, carrying me high up in his left arm, and with his right levelling every man and woman who stood in his way. It was Big Joe carrying me to see his grandson, little Joe; and he bore me off to the poor convulsed boy, and dared me to leave till he was better. He did get better, but Big Joe was dead that night. He had the disease on him when he carried me away from the boat, but his heart was set upon the boy. I never can forget that night, and how important a thing it was to be able to relieve suffering, and how much Old Joe was in earnest about having the doctor."

As time went on, Brown's circle of correspondents widened and included many ministers of the church, university professors, several titled persons, Coleridge and Thackeray, Gladstone, Dean Stanley, and in later years John Ruskin. Many of these expressed great affection. Oliver

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Wendell Holmes ends one letter (1882) "God bless you, dear, good, sweetly human Dr. Brown. Lovingly yours". Mark Twain concludes "Affectionately yours". William Makepeace Thackeray concludes "Farewell and believe me always and affectionately yours". At a banquet given in 1857, Thackeray proposed a toast to "My dear and kind and good old friend, Dr. John Brown". Ruskin began to write letters to John Brown in 1846 and continued till death divided them. They began "My dear Sir", then went through "My dear Dr. Brown" to "Dearest Dr. Brown", and in 1881 one letter ends "Ever your lovingest".

In these letters Ruskin airs his views on the great changes which were taking place in England. "I think" he writes "it admits of much doubt whether not only railroads, but even horses and carriages be not the invention of the Evil One. How much of the indolence, ill health, discomfort, selfishness, thoughtlessness, sin and misery . . . may be referable to the invention of those two articles alone, the carriage and the bridle". He objected to some of the botanical names because he thought them obscene, like orchid and clitoria. Cook's tours, which were becoming very popular, particularly drew his fire—"the stupid tourists let themselves be emptied like coals from a sack at Windermere and Keswick". In another letter he says "German isn't a language at all, but only a throatage or gutterage".

As early as 1835 Brown had periods of depression and self-reproach which became so severe by 1866, after his wife's death, that he gave up practice for a time. Her painful and distressing illness undoubtedly had a part in this, but he worried also about his finances and his spiritual condition.

In 1842 he was bedfast for nearly a fortnight with fever, "but fifteen leeches at my lug did for it, and after four nights of entire sleeplessness, I got some twinklings of oblivion, yet I do not know what it is to get out of my depth". In October 1838 he tells how he had been ill for ten days with a sore throat of sudden onset, and some difficulty in breathing. Three days later he sent for Dr. Scott, because the six leeches he had used the previous day gave him no relief. Two days later they applied twelve leeches behind his ear, still with no result. "Bran poultices everlastingly,—no good." At midnight he sent again for Scott, who bled him sixteen ounces, with instant relief. Ulceration had begun in the throat, and so nitrate of silver was liberally applied. Scott was called again at midnight and bled him until he fainted—about sixteen ounces. "I woke up and saw him brooding over the pulse with a face smiling with perfect delight." . . . "This did the business and all has been easy enough since. It was a queer affair, not a common inflammatory sore throat, but as if a fever had been interrupted, aggravated and destroyed by a virulent sore throat, and then it bled to death. Syme and Scott are looking in".

In 1850 he writes Coventry Dick:

"I have been in indifferent health, my mind is very irritable, many things happening to displease me, some to perplex and distress me. In my profession I was making great progress, getting, I dare say, inflated with silly pride, and in the end of it all, has been an illness of more than a month, sleeplessness, headache, biliosity, rheumatism and a sort of Scotch gout, all running riot in my poor corpus. I am now, however, out of the tempest, feeble but well.

Again, in 1854, "My own profound disrespect and indifferent health and overwork . . . altogether I was in a sorry condition. I am getting old (44) and worn out and tired of this everlasting struggle and worry."

During the end of Mrs. Brown's illness as he watched her gradually fading away, with much suffering, Dr. Brown went his daily rounds with a heavy heart, the sad background of a darkened home always in his thoughts. After her death (1864) he could no longer bear the responsibility of his profession, and left Edinburgh for a few months. For the rest of his life the memory of his happy married years was always with him. His letters were full of sadness. The mystery of sorrow and suffering of his patients weighed heavily upon him, and his own introspection left a deep impression on his daily life. This brooding with overmuch melancholy on the transitoriness of human life, the doubtful honour of a brief passage through a sorry world, and the fear that he had fallen astray in some religious dogma, was built into the germ plasm of his race. Yet these latter years were very productive, and brought him into intimate contact with a great number of the leading minds of his age.

When the periods of depression and hopelessness overtook him, and the goblins of doubt and the imps of despondency were playing Hamlet in his brain in the early morning hours, "There was nothing so comforting to my man-wearied soul as the glorious hills, beautiful exceedingly. As the toilsome years draw home at eventide, who does not find himself near to the unseen."

"Out of his heart God shall not pass,
His image is stamped on every blade of grass".

And for him the two most beautiful words in the English language were "summer afternoon".

Although Brown always shows a great appreciation of the trees and flowers that he passed on his walking tours, there is little said of his own garden, in the heart of the city. Here he spent some of his "spare hours" among his roses, which appear to have been of excellent quality. He was so enthusiastic about these flowers that he went to London to superintend the final arrangements for the first national rose exhibition held in England.

From boyhood he took long walks among the hills and lakes of the neighbourhood. In August 1836 he left the city at three a.m. with his sister Isabella and walked straight through to Callands, six miles away, reading *Comus* aloud as they walked. Edinburgh was not too big for him to flee to the mountains and meres and so satisfy his love of the outdoors. In another letter he

writes "I am going out to Callands today for no other purpose than of being all alone in the open air on the common road for five hours, and have a long and full length *think* with myself".

As he grew older, he stole away in the dark from the world of hurry and doorbells and saw the morning light first sculpturing the outline of "ridge after ridge, misty and tree tufted, stretching away towards the heights, distant and unattainable". Happy the psalmist who could walk with God beside the still waters. "The woods" he said "are the true temple, for there the thoughts are free to mount higher even than the clouds. . . . It is enough to make me repeat after the muezzin in my minaret 'Thank God'."

Almost as soon as he began practice, he contributed articles on general topics to the *Scotsman*, wondering at the time whether they were worth printing. Hugh Miller (Red Sandstone) geologist and editor, sent him twenty pounds, as he was sitting dull and penniless in his London street home, and asked for a continuous flow from his pen for the *Witness*. His own modesty made him hesitate, but Kitty, his wife, grabbed the money, saying "You must write", . . . "If she had not done so, I would never have written a word". These articles were gathered together in 1858 and published under the title *Horæ Subsecivæ*, which he translated "Odds and Ends", "Bye-hours", or "Brown Studies". In his preface he thought they were "perhaps a sort of compromise of flesh and fowl, like the duck-billed platypus; neither not medical enough for doctors, nor too medical for their patients". Five hundred copies out of the thousand printed were sold in a week, and a second edition was issued. A second series appeared in 1861, followed by a third in January 1882, so popular that it required a second edition in March. The contents of these three volumes touch on many subjects; let us look first at some of his personal opinions which crop up occasionally.

Brown had strong objections to the cramming system that obtained in the medical schools of that day, and unfortunately is still far too prevalent. He quotes from Epictetus; "As if sheep, after they have been feeding, should present the very grass itself, which they cropped and swallowed, instead of concoting it into wool and milk". He was steeped in the medical philosophy of the time and cites Radcliffe; "When young I had fifty remedies for every disease; when old I had one for fifty". And Gregory; "Young men kill their patients, old men let them die". He advised the young practitioner to cultivate stereoscopic thinking—viewing subjects as well as objects with our own two eyes—a maxim most useful in this mechanical age of medicine. System is not always method, much less progress. However, all his dicta have not stood the litmus of time so well. He thought that obstetrics (man midwifery) has been a greater evil than good. It was first brought into use when the Grand Monarque, to conceal the shame of La Valliere, sent for M. Chison, instead of the customary *sage-femme*. He pays a great tribute to the country doctors of his neighbourhood, and names several of them. One was Clarkson of Selkirk, who was the original of Gideon Gray, in Scott's *Surgeon's Daughter*. He advocated free competition in medicine, as suggested by Alan Smith, by which he meant that a medical degree should not be necessary for practice—that a man should be allowed to choose his own doctor, as he does his own wife or tailor. A license to practice constitutes a virtual monopoly.

He held the opinion that the Maker of our beards knew what He was doing, and therefore we should escape the misery, expense and loss of time in shaving. He dared to hazard the theory that no hair of the head or beard should be cut—"or needs it any more than the eyebrows or eye-lashes". Toothbrushes he considered not necessary for health—quite a modern idea too. He hated false teeth and thought that rheumatism was best treated by patience, flannel and six weeks. Wigs were just beginning to pass out of fashion and Brown would like to hasten their exit. Brown's pathology was imaginative and highly speculative. But in his lectures to working people, he spoke plainly and sincerely, and hoped that by following his advice they might have their eyes closed by the fingers of their great-grandchildren!

The Doctor was always fond of dogs, but owned the first only when he was at college. His brother picked up Toby for two pence from some boys who were trying to drown him in Lochend Loch. They kept him for weeks in the house unbeknown to anyone but the cook. One night when Father Brown was bathing his feet in the bedroom, Toby introduced himself "with a wag of his tail" intimating a general willingness to be happy. "My father laughed most heartily—and gave such an unwonted shout of laughter that the rest of the family rushed in to see what the matter was . . . and Toby became an accredited member of the family."

Writing in 1881 he says:

> "Our present dog is Bob the Fourth. Bob the First sleeps in a hole in Badenoch, slain in fell battle with a badger, as fine and game a little soul as ever was in a body. The third Bob was a perfect Dandie, wretchedly murdered by some miscreants in Fisherrow Harbour; I wish I had the scourging of them for ten minutes every second day for a month. The fourth cost me fifty shillings when quite young and before having distemper. My only orders to Mr. Lang, the breeder of Dandie Dinmounts were 'Let him be pure and big'."

When Bob arrived on a chain, he was in a great state of consternation. When Dr. Brown took off his collar Bob ran out the door, with the Doctor hurrying after him along Princess Street. After some hours, there he was on George Street, tongue out and wearied. The moment he eyed his future master, off he went again.

Brown observed that there was character in dogs, just as in humans, "There goes good John"

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he said, "which people call a magnificent St. Bernard, but he is a complete intake, like many men and some women. He has a good face, handsome figure and no brains worth mentioning." Another dog he called conscientious; when his muzzle came off, he brought it home in his mouth. He quotes: "Man is the God of the dog, it were well if we served our Master as our dog serves us" . . . "The misery of dogs is that they die so soon", or as Sir Walter says; "It is well they do, for if they lived as long as a Christian and we liked them in proportion, and then they died, that was a thing we could not stand".

Rab, perhaps the best known dog in the English-speaking world, never belonged to Brown, but Rab was Rab, more emphatically Rab than a dog. The story of this huge mastiff is one that can never be retold and retain the beauty and pathos of the original. Two boys on the road home from school saw a crowd gathering and ran to see what was the matter. Poor Rab was being assaulted by a bull terrier who was slowly making his way up the neck. The boys peeped under the legs of the men and saw that Rab was muzzled! With a sharp knife one of them (Brown?) crawled close enough to cut the leather of the muzzle, and one shake of Rab's mighty head spelled the end of the terrier. Little did young Brown think that some day he would tell a tale which would make Rab's name famous all over the world!

Years passed quickly. In his haughty way, Rab considered Brown his friend, whenever they met. John finished the High School and entered as a medical student in Minto House, which was now the private hospital of Mr. Syme. One October afternoon just as John was leaving, the gate opened and in walked Rab, followed by Jess, the donkey, with James, the Howgate carrier leading her.

In the cart was the mistress "with a trouble in her breast, some kind of an income, we're thinkin' ". The anxious, pale, lovely face of the woman told the tale. "Allie" said James, "this is Maister John, the young doctor, Rab's friend, ye ken. We often speak about you, doctor".

Then came the operation, without chloroform, and the medical students crowded around the operating room. Behind the table was James sitting down with Rab's huge and noble head between his knees. The brave patient was still and silent through the swift and bloody operation. Rab's ears were up, and he gave deep growls and impatient yelps. The operation over, Allie stepped off the table, curtsied, and in a low clear voice begged their pardon if she had behaved ill. Even the students wept like children.

Allie was put to bed, and James became her nurse, never leaving her side. Rab also was there. Four days later the dreadful hospital infection set in, with its fever, delirium and death. In the dim morning, after a heavy fall of snow, James brought Jess and the cart, wrapped the body carefully in the blankets that had been a wedding-present, and carried her tenderly to the cart. Taking Jess by the head he moved away through the shadows, Rab following behind. Next day the neighbours standing near saw him lower the body into the bleak, ragged hole in the spotless snow. Shortly after James fell ill and was unconscious when the doctor came, dying quite suddenly.

Then there was Jeems, the doorkeeper of his father's church in Edinburgh, a misshapen little man, age and name unknown ("why should he have a surname? Abraham got along without one"). "His face was so extensive and met you so formidably and at once, that it mainly composed his whole". As Sydney Smith once said of a quarrelsome man. "His very face is a breach of the peace". And Madame Sievieгne of another "He abused the privilege men have of being ugly". The rest of his body was scrimpy, his legs the shortest. Emphasizing his deformity, he wore a long blue greatcoat "made for a much taller man, and its tails resting on the ground, with its large hind buttons in a totally preposterous position". But he was a man of authority in the Church, feared but respected for his sharp tongue. "One day, a descendant of Nabal, having put a crown piece into the plate, instead of a penny, and staring at its white and precious face, asked to have it back, and was refused. . . . "In once, in for ever." "Aweel", grunted he "I'll get credit for it in heaven". "Na, na", said Jeems, "ye'll get credit for only a penny"!

In the days of tight lacing and ill ventilation, fainting in church was a common occurrence among the "young huzzies" as Jeems called the servant girls. He generally came for Dr. John, who was a regular attendant at his father's church, and who taught him the propriety of laying the young ladies flat on the floor and relieving them by cutting their stay-laces, which cracked like a bow string. But one day a young lady was slow in coming to. Jeems came to the Doctor with that huge, terrifying visage and his open "gully" in hand, whispering "Wull 'oo ripp her up the noo?" The story of this singular and devout man is one of great pathos, and one of Brown's best.

Another of his sketches was of a remarkable child, Marjorie Fleming, beloved of Sir Walter Scott and everyone else who knew her. She lived near Sir Walter in Edinburgh and he visited her nearly every day. Often he wrapped her up in his plaid and carried her into his own house and into the room where he wrote many of his novels. She was a most precocious child, with amazing power over Sir Walter. At seven she could recite parts of *King John,* till Sir Walter "swayed to and fro, sobbing his fill".

Her diary and many of her little poems have come down to us, and form the basis of this essay, written about fifty years after Marjorie's death, aged eight, of measles. Next to *Rab* it is the best example of Brown's art of story telling.

At six, she wrote a letter to her sister Isa, in which she says:

"This is the first time I ever wrote a letter in my life. There are a great many girls in the Square, and they cry just like a pig when we are under the painful necessity of putting it to death. Miss Portune, a lady of my acquaintance praises me dreadfully. I repeated something out of Dean Swift, and she said I was fit for the stage, and you may think I was primmed up with majestic pride, but upon my word, I felt myself turn a little birsay—birsay is a word, which is a word that William composed, which is as you may suppose, a little enraged. This horrid fat simpleton says that my aunt is beautiful, which is intirely impossible for that is not her nature."

When she was on holiday at Braehead she kept a diary. Here are some extracts:

"The day of my existence has been delightful and enchanting . . . Mr. Craky and I walked to Craky Hall hand in hand in innocence and metitation sweet thinking on the kind love which flows in our tender hearted mind, which is overflowing with majestic pleasure no one was ever so polite to me in the hole state of my existence."

"I confess I have been very more like a little young devil than a creature for when Isabella went upstairs to teach me religion and my multiplication and to be good and all my other lessons, I stamped my foot and threw my new hat which she had made on the ground and was sulky and was dreadfully passionate." . . . "I am now going to tell you the horrible and wretched plague that my multiplication gives me you can't conceive it is the most devilish thing is 8 times 8 and 7 times seven is what nature can't endure." . . . "As this is Sunday I will meditate upon sencible and religious subjects First I should be very thankful that I am not a beggar." . . . "I am very sorry to say that I forgot God—that is I forgot to pray today and Isabella told me that I should be thankful that God did not forget me—or if he did O what would become of me if I was in danger and God not friends with me. I must go to unquenchable fire and if I was tempted to sin—how could I resist it O no, I will never do it again—no, no, if I can help it." . . . "An annibaptist is a think I am not a member of—I am not a Pisplekan just now, and a Prisbeteran at Kirkcaldy, my native town. . . . The hedges are sprouting like chicks from the eggs when they are newly hatched, or as the vulgar say, *clacked*. . . ." "Dr. Swift's works are very funny. I got some of them by heart."

Although in 1836 Brown meditated sometimes on a medical book, "which I mean to write for my own and not for the public good", nothing came of it perhaps because, as he once said, "his constitution could stand a great deal of ease". However, two years later, he had an idea of a treatise on pain and "something on the essential and irreconcilable difference between medicine and all the other sciences", but his practice was increasing. Edinburgh University had given him an F.R.C.P. and appointed him librarian. At the same time his life of authorship began, so we hear no more of the work on medicine.

One of the incidents in his early life which may partly account for the melancholia that continued to assail him, was the death of his mother when he was five years old. "My love of my mother" he writes "has been unsatisfied in me for twenty-eight years. I can remember standing at her grave, until the men began pulling from me the little cord I held in my hand holding the coffin". Fortunately, in the last few years this oppression seems to have left him. "I have given up now inquiring nicely into the state of my soul, and I am so utterly at sea in all attempts to make out the mystery of myself—wherein I am good and wherein I am desperately wicked". He was able to use his pen freely to the end, but in April 1876, because of a recurrence of his nervous illness, he wrote a circular stating that he was discontinuing ordinary medical practice. His friends felt this was the time to give some practical demonstration of their affection, and presented him with a testimonial in money. But his days were spent much as before, still taking care of some of his old friends, enjoying the summer months by the Spey or the Tweed.

On May 5, 1882, Dr. Brown spent the morning as usual among his friends, and in the evening was in his chair in the drawing-room, reading aloud some sentences from the book which interested him most at the time. Next day he stayed in bed for he "felt he had caught cold". It was only too evident that pneumonia, the kindly friend of the aged, had supervened, and in a few days he died. His body rests in New Calton Cemetery, beside those of his father, wife and infant daughter.

And now, three-quarters of a century later, his voice prisoned in the silent pathways of the night, we can recall him as a man whose charm was the essence of his personality. Although he was not one of those rare and original men who holds discourse with the universe at first hand, he had a way with the beautiful and perfect word, and like Hudson, the supreme gift of disclosing not only what he saw, but the spirit of his vision. Neither money-making nor the bubble reputation came much into his thoughts, nor was he dazzled by life's glitter and pretensions. Although he had many interests outside of medicine, he seems never to have been seduced into neglecting his professional work. We still think of him as an able physician, a sympathetic writer and an esteemed friend whom we delight to honour.

ASSOCIATION NOTES

CANADIAN MEDICAL ASSOCIATION ANNUAL MEETING, BANFF, ALBERTA

June 9 to 13, 1952

Once in about every ten years the doctors of Alberta have the pleasure of being hosts to the Canadian Medical Association, and this is one of those years. The members of the Division look forward to meeting old friends from all parts of Canada and making many new ones. We

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hope that you will plan to come and enjoy a week of healthful recreation in the midst of an unsurpassed and unspoiled natural landscape.

It is difficult to describe adequately the superb scenic setting of Banff, but it is impossible to be unmoved by its irresistible charm. Within view of this famous mountain resort, nestled in the green valley of the Bow River, are several fine peaks – Cascade, Rundle, Norquay, Aylmer, Stoney Squaw, and Sulphur. Peeping out from behind these are scores of glittering peaks beckoning, as it were, to the visitor. A motor tour of this area might also include such popular places as Sundance Canyon, the Golf Course, Bow Falls, Upper Hot Springs, the Wild Animal Paddock, the Fish Hatchery, and those weird examples of nature's sculpture, the Hoodoos—to mention only a few nearby places of interest.

A ten-minute drive from Banff takes the visitor to the Mount Norquay Lodge on the slopes of Mount Norquay. In another ten minutes he can reach the 7,000 foot level on a spectacular chair-lift, rising through a vertical distance of more than 1,300 feet. The beauty of the surrounding panorama is breath-taking; snow-capped peaks glistening against a blue sky, lacy mountain streams dropping into tiny lakes, and colourful forest-clad mountain slopes where bighorn sheep, Rocky Mountain goats, moose and deer are frequently observed. For those who prefer to do their mountain climbing in comfort, the chairlift is a new and exciting experience.

(Courtesy of Canadian Pacific Railway Company)
Putting Green—Lake Louise and Victoria Glacier, Alberta.

As to the meeting itself, it has been arranged for the Council Sessions to be held on Monday and Tuesday, June 9 and 10, with the annual dinner to Council taking place on Tuesday evening. The scientific sessions start on Wednesday morning, and you will probably desire to arrive on Tuesday or early Wednesday morning; although undoubtedly many will arrive over the week-end in order to have a few free days before the scientific sessions commence. If you have not already done so, please make your hotel reservations now, using the application form which has been printed in recent numbers of the Journal. Fill in one of them and mail it to Dr. A. E. Wilson, 904 Greyhound Building, Calgary. If you are making other plans for your accommodation, please write Dr. Wilson anyway, as the housing committee will want to know about your presence, even though you are not living in the Banff Springs Hotel or the Chateau Lake Louise.

Both the Banff Springs Hotel and the Chateau Lake Louise have been taken over for the week and will operate as one hotel. Meals may be taken in either hotel and all meals are included in the daily rate; $13.50 per person two in a room, $16.50 one in a room. There will be a bus service on the hour between the two hotels, charge $1.00 per trip each way.

The scientific program is of the conventional type; no new ideas have been introduced in its planning, but its quality is very high and it should have a good general appeal. There will be four Round Table Discussions each morning followed by three outstanding papers in General Sessions. Thursday afternoon is free for golf, swimming, riding, mountain tours, canoeing, shopping or whatever you fancy; but on both Wednesday and Friday afternoons there will be a Session A for Medicine and related subjects and a Session B for a group of papers in the various fields of surgery. On both afternoons there will be sectional meetings too. Our guest speakers will include at least one from England and three from the United States. A business meeting of the section on General Practice is planned for Thursday evening.

Arrangements for the Physicians' Art Salon are well under way and it is hoped that this splendid feature will be housed in the Banff Springs Hotel.

There will be a large commercial exhibit in which seventy-eight booths will be occupied and many of the firms will have their senior executives present.

The golf committee is active and play for the Ontario Cup and the Alberta Cup will be outstanding features.

On the distaff side plans for entertainment are in progress and it is hoped that a record number of wives will come along with their husbands. Scenic excursions through the mountains by car, bus, boat, and chairlift will give the visitors a chance to see the Rockies in all their variety and magnificence. The Banff Springs golf course stretching along the Bow River below the hotel will be the site of the women's golf competition and it is expected that all the ten provinces will be represented in the play. Swimming, riding, canoeing, a luncheon at beautiful Lake Louise, a glimpse of Alpine meadows, and tea on top of a mountain are all listed as possibilities and the ladies' committee are finding it difficult to decide what to leave out since there will not be time for everything.

For parents who plan to bring along the children a special committee has been appointed to look after the children's entertainment in order to free their parents for convention activities.

This will be a fine opportunity for you and your wife to renew old friendships and make many new ones. Do come.

Preliminary Program

Canadian Medical Association

EIGHTY-THIRD ANNUAL MEETING

BANFF, JUNE 9 – 13, 1952

President—Dr. Harcourt B. Church, Aylmer, Que.
President-Elect—Dr. Harold Orr, Edmonton.
General Secretary—Dr. T. C. Routley, Toronto.
Deputy General Secretary—Dr. A. D. Kelly, Toronto.

(This meeting is held in conjunction with the 47th Annual Meeting of the Alberta Division.)

Arrangements for the Eighty-third Annual Meeting to he held in Banff, Alberta during the week of June 9 are proceeding satisfactorily. General Council will meet on Monday and Tuesday, June 9 and 10. A series of Round Table Conferences has been arranged for the mornings of Wednesday, Thursday and Friday, from 9.15 a.m. until 10.30 a.m., to be followed by General Sessions. There will be sectional meetings and sessions of a more general nature on the afternoons of Wednesday and Friday. The Annual General Meeting will be held on Wednesday evening, June 11, at 8.30 o'clock. On this occasion the retiring President, Dr. Harcourt B. Church, will hand over the badge of office to Dr. Harold Orr.

Wednesday, June 11, 1952

ROUND TABLE CONFERENCES

9.15 a.m.

Ante-Partum Hæmorrhage in the Third Trimester.
Dr. T. R. Clarke, Edmonton.

Burns.
Dr. A. R. Tilley, Toronto.

Rheumatic Fever in Children.
Dr. Howard Spohn, Vancouver.

The Place of Preventive Medicine in General Practice.
Dr. F. W. Jackson, Ottawa.

GENERAL SESSION

10.45 a.m.

Valedictory Address.
Dr. Harcourt B. Church, Aylmer, Que.

The Present Status of Anti-coagulants in Thrombo-embolic Disease.
Dr. E. S. Mills, Montreal.

The Blackader Oration.
Dr. R. W. B. Ellis, Edinburgh.

Session A

2.00 p.m.

Diagnosis and Treatment of Headache.
Dr. R. K. Thomson, Edmonton.

Recent Advances in Pædiatrics.
Dr. Charles Read, Winnipeg.

The Relationship of Immunization Procedures to Poliomyelitis.
Dr. A. J. Rhodes, Toronto.

Diagnosis and Treatment of Leucorrhœa.
Dr. George B. Maughan, Montreal.

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Session B

2.00 p.m.

The Early Diagnosis and Treatment of Breast Tumours.

Dr. James W. R. Rennie, Winnipeg.

The Management of Complications in Biliary Tract Surgery.

Dr. C. H. Crosby, Regina.

Inguinal Hernia.

Dr. E. F. Ross, Halifax.

Lung Abscess.

Dr. Jacques Bruneau, Montreal.

SECTIONAL MEETINGS

Section of Anæsthesia

2.00 p.m.

Anæsthesia for the Patient with a Complicating Disease or Condition.

Dr. E. A. Gain, Edmonton.

Spinal Anæsthesia in General Practice.

Dr. R. J. Fraser, Hamilton.

Anoxia.

Dr. W. M. Hall, Vancouver.

Local Anæsthesia for the Upper Extremity.

Dr. R. P. Douglas, Calgary.

Section of Psychiatry

Present Day Trends in Regulations Governing Admission to Psychiatric Hospitals.

Dr. R. R. MacLean, Ponoka.

The Place of the Psychiatrist in the Community Medical Service.

Dr. R. O. Jones, Halifax.

Stress Dynamics in Psychiatric Perspective.

Dr. H. E. Lehmann, Verdun.

Mental Hygiene in a Health Unit.

Dr. H. Siemens, Edmonton.

Section of Radiology

Treatment of Hæmangiomata.

Dr. Jean Bouchard, Montreal.
Dr. Carleton B. Peirce, Montreal.

The Significance of Solitary Shadows in the Chest Film.

Dr. A. Turnbull, Vancouver.

Osteoid Osteoma.

Dr. K. F. MacEwen, Toronto.

How the Radiologist can Co-operate in the Management of the Long Intestinal Tube.

Dr. R. A. Macpherson, Winnipeg.

Thursday, June 12, 1952

ROUND TABLE CONFERENCES

9.15 a.m.

The Place of the General Practitioner in Industry.
Dr. Gordon A. Sinclair, Toronto.

Acute Upper Respiratory Infection in Children.
Dr. J. Harry Ebbs, Toronto.

Recent Advances in Treatment of Prostatic Carcinoma.
Dr. John Balfour, Vancouver.

Fractures and their After-Care in General Practice.
Dr. Leslie Black, Toronto.

GENERAL SESSION

10.45 a.m.

Applied Psychiatry in General Medicine.
Dr. Franklin Ebaugh, Denver, Colo.

Simple Measures in the Prevention and Treatment of Asphyxia Neonatorum.
Mr. G. F. Gibberd, London, England.

Alcoholism.
Dr. Gordon Bell, Northmount, Ont.

THURSDAY AFTERNOON FREE FOR RECREATION

Friday, June 13, 1952

ROUND TABLE CONFERENCES

9.15 a.m.

The Place of the Physician in Civil Defence.
Dr. R. MacGregor Parsons, Red Deer.

Chronic Diarrhœa in Adults.
Dr. J. Wendell MacLeod, Saskatoon.

Pancreatitis.
Dr. Hugh Stuart, Calgary.

When is an Ovarian Cyst Really a Surgical Problem?
Dr. Brian D. Best, Winnipeg.

GENERAL SESSION

10.45 a.m.

Appendicitis.
Dr. Campbell Gardner, Montreal.

Recent Advances in Dermatology.
Dr. George Lewis, New York.

Evaluation of Newer Drugs in the Treatment of Peripheral Arterial Disease.
Dr. R. B. Kerr, Vancouver.

Session A

2.00 p.m.

Evaluation of Liver Function.
Dr. R. E. Bell, Edmonton.

Recent Advances in Radiotherapy.
Dr. Ivan H. Smith, London.

Consideration of the Retroverted Uterus as a Normal Position.
Dr. Irving A. Perlin, Halifax.

Radioactive Isotopes in Medicine.
Dr. John Gemmell, Winnipeg.

Session B

Use and Misuse of the Walking Plaster Boot.
Dr. O. Rostrup, Edmonton.

Experience with Carcinoma of the Large Bowel.
Dr. C. W. Harris, Toronto.

Management of Closed Head Injuries.
Dr. G. K. Morton, Edmonton.

The Diagnosis and Treatment of Polypi of Colon and Rectum.
Dr. J. L. Petitclerc, Quebec.

SECTIONAL MEETINGS

Armed Forces Medical Section

2.00 p.m.

Defence Medical and Dental Services Advisory Board.
Dr. E. A. McCusker, Ottawa.

The Defence Research Medical Laboratories—Their Character and Opportunities.
Dr. M. G. Whillans, Toronto.

Medical Services in Korea.
Major E. H. Anderson, R.C.A.M.C.

Progress Report, the Medical History of the War.
Dr. W. R. Feasby, Toronto.

Section of Historical Medicine

History of Specialism and its Implications for Today.
Dr. H. E. Rawlinson, Edmonton.

Early Medical Education in North America.
Dr. H. E. MacDermot, Montreal.

Dermatologic Commentary in English Literature.
Dr. D. E. H. Cleveland, Vancouver.

Early Medical Explorers in the Rockies.
Dr. D. A. McKenzie, Banff.

Section of Ophthalmology and Otolaryngology

Orbital Complications of Sinus Infection.
Dr. K. A. C. Clarke, Edmonton.

Cortisone in the Treatment of Eye Disease.
Dr. H. L. Ormsby, Toronto.

Hoarseness.
Dr. D. S. Gorrell, Calgary.

The Care of the Eyes of the Newborn.
Dr. E. F. Foy, Edmonton.

A LETTER TO THE LADIES

The ladies of Alberta are looking forward to the pleasure of greeting the wives of the doctors of Canada next June at Banff. I cannot imagine a more beautiful setting for the meeting than this famous park of some 2,500 square miles, and containing scores of renowned points of interest. The view from the top of Mt. Norquay, easily reached by chair-lift, is breath-taking. The amenities of our two hotels, the Banff Springs and the Chateau Lake Louise will appeal to the most fastidious, while for those who prefer a more out-of-doors holiday, all sorts of accommodation is available.

The Ladies' Committees are making plans for your pleasure but there will not be too many organized affairs. You can follow your own bent as much as you desire.

Perhaps you were wondering about the weather. The days in June will be long and reasonably warm but not too hot. You will need a warm suit and a light coat as the evenings are cool. Formal dress is usually worn for Wednesday evening functions.

Come prepared for your favorite recreation. Bathing in the Mineral Hot Springs, boating, mountain-climbing, fishing, golf, hiking, photography, tennis, trail-riding, or you may just sit about in a beautiful environment, meeting old friends and making new ones from all parts of Canada.

MARGARET ORR

MEDICO-LEGAL

LOST INSTRUMENTS

T. L. FISHER, M.D.,* Ottawa

When one thinks of foreign objects being left in wounds or in body cavities sponges come to mind first. That sponges are lost so seldom is a tribute to the methods of sponge counts and the accuracy with which they are done in countless operations. In Canada the Canadian Medical Protective Association has knowledge of only three cases in which instruments were allowed to remain in the body cavities. The first and most startling occurred some years ago. A large spatula, 10 or 11 inches long, was being used during the closure of a very obese abdomen. Somehow or other it slipped into the abdomen and its loss was not noticed. When later the patient complained of difficulty bending and straightening an x-ray examination of the abdomen was undertaken. The spatula was found lying in the right side of the abdomen in just the position which would make movement painful. So unusual was the case that no repetition was foreseen. During the past year however two more cases in which instruments were left in the abdomen have come to the Association's attention.

Early in 1951 a surgeon reported to the Association that after cholecystectomy in October 1950 one of his patients had had a difficult postoperative course and continued to have abdominal pain over the next three months. In

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January 1951 he was referred to a sanatorium for chest examination and during the x-ray examination the presence of a hæmostat in the upper abdomen was noted. The surgeon promptly notified the patient of the finding, advised immediate removal and with the patient's full consent removed the hæmostat. Complete recovery followed.

Just a month later another surgeon consulted the Association about a somewhat similar case. His patient had been under treatment from 1949 for gastric distress and food intolerance. In July 1950 repeat x-ray studies showed a duodenal ulcer and she was advised to have a gastrectomy done. Recovery from the operation was uneventful, the patient left the hospital on the tenth postoperative day and was able to return to her home less than two weeks later. Apparently there were no untoward symptoms for five months when the patient began to have indigestion again. That was followed by vomiting and the emesis contained frank blood.

The patient was referred back to the surgeon who found, on x-ray examination, a hæmostat in her right lower quadrant. The surgeon advised its removal, consent was obtained and it was removed. Convalescence was uneventful and subsequent health was good.

In neither case did there seem to be any extenuating circumstances. Expert surgical advice as well as legal advice was to the effect that there was no hope for successful defence, that the cases should go to court only if the financial demands of the patient were unreasonable. Both patients demanded little more than reimbursement for actual out-of-pocket expenses, so settlement was possible in the first case for $3,300.00 and in the second case for $3,500.00.

When once there is a realization that instruments can be and have been lost and consideration is given to the whole subject, it seems rather remarkable that more cases have not occurred. The number of instruments used, during an abdominal operation for example, the various sizes of the instruments, the fact that they are used often deep in body cavities where they can become completely hidden from view, and the fact that more than one person may be responsible for placing them in position, suggests that the loss of one could occur more easily than is realized. How best to prevent similar accidents poses a problem. Among the surgeons consulted by the Association there was unanimity that a count of instruments similar to sponge counts is not feasible. The Association learned that in one or two hospitals patients who have had surgery in a body cavity are x-rayed on their way from the operating room to their beds. One of the two surgeons whose cases are quoted has established this as a routine in all his cases. Perhaps this precaution should become routine. Until it does surgeons should take advantage of the fact that instruments are hard and unyielding and therefore usually may be felt easily. A thorough and meticulous search of the operative area, even if done quickly, should prevent accidents of this kind.

*Secretary-Treasurer, Canadian Medical Protective Association.

SPECIAL CORRESPONDENCE

The London Letter

(From our own correspondent)

HEALTH SERVICE CHARGES

With an annual bill of over £50,000,000 for prescriptions it was inevitable that the Chancellor of the Exchequer should decide to make the pruning of this item one of his major aims in the slowing up of expenditure on the National Health Service which has been imposed on the Government by the present financial state of the country. The new National Health Service Bill which is now before Parliament aims at reducing the cost of the Service by £20,000,000. This reduction is to be achieved in three main ways.

In the first place a charge of 1s. is to be made for each prescription form issued, irrespective of the number of prescriptions on the form. People in receipt of national assistance, or their dependents, and war pensioners, in respect of "accepted" war disability, will be able to claim repayment of this charge. The saving to the Service is expected to be £12,000,000 a year. A charge, up to half the cost, is to be made on certain appliances, such as surgical belts and boots, elastic hosiery, hearing-aids and wigs, when supplied to hospital outpatients. This will bring in £500,000 a year. The second lot of charges to be made falls on the dental service, and £1, or the full cost if less than £1, is to be made for a course of dental treatment. This is in addition to the charge for dentures which was imposed by the last Government. Children under the age of 16 years, children in full-time attendance at school, expectant mothers and mothers who have had a child within twelve months, will be exempt from this charge which is expected to bring in £7,500,000 a year. Finally, the present charge for "amenity" beds is to be doubled, and local health authorities are authorized to charge for the use of day nurseries.

Not unnaturally, these proposals have provoked a howl of resentment from the party now in opposition, and the medical and pharmaceutical professions have not been slow to point out the administrative difficulties involved. Informed opinion, however, is agreed that, clumsy though the method may be, the Government had no alternative. As a short-term policy to deal with a current emergency, it is fully justified, but there are many who are hoping that those now in authority will be able to produce, in due course, a more constructive plan for so modifying the National Health Service as to give some guarantee that (a) the country can afford it, (b) there will be an appreciable beneficial effect on the health of the country.

GREAT ORMOND STREET

It is not only in this country that "Great Ormond Street" is synonymous with all that is best in pædiatrics. The Hospital for Sick Children, to give it its official title, has now attained centenarian status, and centenary celebrations are to be held later in the year. It was on Valentine's Day, 1852 that the Hospital was opened at 49 Great Ormond Street, as the results of the persistent efforts of Dr. Charles West. From the original 10 beds, which constituted the entire inpatient accommodation of the original hospital, there has been a steady increase through the intervening century. In 1877 the hospital

moved into new premises, with 120 beds. Ten years later even this accommodation was inadequate, and in 1887 the children of the Empire, to celebrate Queen Victoria's Jubilee, contributed the funds which allowed of the erection of new buildings, with accommodation for 240 beds. Half a century later King George VI and his Consort opened the present buildings. Further expansion has been delayed by the 1939-45 war and its aftermath, but it is hoped that new accommodation will soon be available and that part of the centenary celebrations this year will be the laying of the foundation stone of a new outpatient department. "Great Ormond Street", as is only appropriate in a children's hospital, has always retained that attribute of its distinguished benefactor, Sir James Barrie which he immortalized in "Peter Pan". As it enters upon its second century it does so with a youthful enthusiasm and also the good wishes and congratulations of all who are concerned with the welfare of children.

Diphtheria Immunization

A recent issue of the *Monthly Bulletin of the Ministry of Health* contains a report on an investigation into the cause of the disquieting decrease in the number of children being immunized against diphtheria. In 1950, 141,000 fewer children under five years of age were immunized than in 1949. The aim of the Ministry has been to immunize 75% of children before their first birthday, this being recognized as the lowest percentage necessary to keep diphtheria under control. In May, 1951, however, less than 50% of children under nine months to one year had received their first injection. Apathy on the part of parents would appear to be the main cause for this decrease in immunization. Typical of the reasons given for not having their children immunized were: "Not bothered"; "Never heard of it"; "Father does not agree". Presumably this attitude is largely due to the very success of the immunization scheme, with the resultant disappearance of diphtheria as a serious public health hazard. As *The Times* points out in a leading article, however, "it will be a serious matter if apathy ruins one of the most successful and life-saving public health achievements of recent years".

London, March, 1952. William A. R. Thomson

OBITUARIES

LE DR Z.-M. AUMONT, décédé à Montréal, le 19 janvier à l'âge de 79 ans.

Né à Saint-Alexis, comté de Montcalm, le 3 janvier 1883, le défunt avait fait ses études classiques au collège de L'Assomption et ses études médicales à l'Université Laval. Il avait pratiqué la médecine pendant plus de 40 ans à Montréal et dans le village de Saint-Jean de Matha, près de Joliette. Le défunt laisse deux fils.

DR. WALTER LINLEY BARLOW, died on January 21 in the Montreal General Hospital in his 78th year. He was connected with the General Hospital for 44 years and was the head surgeon at the time of his retirement. Born in Montreal, he obtained his B.A. degree at McGill University and entered the medical science.

He trained as a surgeon under Dr. George E. Armstrong and pioneered in the x-ray field. Dr. Barlow did x-ray work at the hospital before a department was set up to handle this phase of medicine. His x-ray research was responsible for the amputation of a number of his fingers through destruction caused by the rays. He was a member of the C.M.A., the Montreal Medico-Chirurgical Society, and the Royal College of Physicians and Surgeons of Canada.

DR. EDGAR ALEXANDER CAMPBELL, aged 61, died on January 17 in Deer Lodge Military Hospital, Winnipeg, where he was a member of the medical staff. Born in Melita, Man., he graduated from Manitoba Medical College, then served overseas in the first world war. On his return he practised in Melita for eight years then moved to St. James and for eight years was on the staff of Deer Lodge Hospital. He was a past master of Oriental Masonic Lodge, Melita, and was a member and elder of St. James United Church. His widow, a daughter, a son and one grandson survive him.

DR. VERNON HAROLD CRAIG, former president of the Ottawa Academy of Medicine, died on January 29 in his 67th year. Born at Ashton, Ont., he graduated in Arts from Queen's University in 1908 and from the Medical School in 1912. After receiving postgraduate training in New York City he set up practice in Westboro just prior to World War I. At the outbreak of war he joined the R.C.A.M.C. At the cessation of hostilities he returned to Ottawa and practised there until the time of his death. Surviving besides his widow are two sons.

COL. ALAN LESLIE DELAHAYE, aged 62, head of medical administration at Queen Mary Veterans' Hospital, Montreal, died on January 27. Born at Pembroke, Ont., he studied medicine at McGill University and interned at Royal Victoria Hospital. He took postgraduate work in Edinburgh, London and Vienna.

He served overseas as a medical officer in the First World War, after which he returned to private practice. In the Second World War he served as a major as an eye, ear and nose specialist on various boards in Military District 4. Later he was promoted colonel and headed medical boards in the district. He is survived by his widow.

DR. DAVID LEVERN DICK, aged 69, who has practiced medicine in Vancouver for the past four years, died in St. Paul's Hospital on January 18. Born in Thamesville, Ont., and a graduate of Toronto University in 1911, Dr. Dick practiced in and around New York City for a few years after graduation. He later moved to Galahad, Alberta, and came to Vancouver four years ago. He is survived by his widow.

DR. PERCY N. GARDNER, aged 67, died on February 4 at Toronto Western Hospital following a coronary thrombosis. Dr. Gardner was in charge of hospital inspection for the Provincial Department of Health.

Born in Winnipeg, he graduated from the University of Toronto in medicine in 1909. He was assistant coach for the Varsity football team from 1907-1910 and appointed University of Toronto football team physician in 1910.

After graduation, Dr. Gardner established a practice in Windsor. Returning to Toronto in 1930, he practiced there until appointed to the Provincial Department of Health. Dr. Gardner was a noted swimmer and a champion driver. He leaves his widow and one son.

DR. FREDERICK WILLIAM GREEN, aged 74, prominent and highly respected Glace Bay, N.S., practitioner died on January 25 at the Glace Bay General Hospital where he had been a patient for upwards of one year. A native of Pictou County, he graduated as a doctor of medicine at McGill University, in 1902 and shortly afterwards came to Cape Breton. For upwards of 50 years he served the people of Glace Bay and district faithfully and well. Quiet and gentlemanly in all his associations Dr. Green represented the finest traditions of his profession. His health began to fail about two years ago and early last year he entered the General Hospital where he remained a patient since. Dr. Green is survived by his widow and a daughter.

DR. NORMAN B. GWYN died in Sunnybrook Hospital on February 1. He had been in poor health for over a year and, in the last six months, he was a very sick man. He had been entrusted with the preparation of a paper on the Faculty of Medicine for the Centenary celebration of the University of Trinity College last summer and exhausted himself in the effort. Hospital care became necessary several weeks ago.

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Dr. Gwyn was born in Dundas, Ont., in 1875. He attended the Collegiate Institute in Hamilton and graduated M.B. University of Toronto in 1896. He took an extensive postgraduate training in Germany and at Johns Hopkins where his uncle, the late Sir William Osler, was chief in medicine. His first practice was in Philadelphia. He bore a striking physical resemblance to his celebrated uncle, and conscientiously sought to emulate his distinguished relative in professional attainment and in literary studies. More than one hundred contributions on scientific subjects were published in German, American and Canadian journals. He was an enthusiastic charter member of the Medical History Club.

Dr. Gwyn served with distinction in World War I. For a considerable time he was in charge of the Medical Service of No. 1 Canadian General Hospital in France and reached the rank of Lieut.-Col. After the war he began practice in Toronto and was consultant physician in Christie Street Hospital and member of staff in Toronto General Hospital. He was an active Fellow of the Academy and, in later years, donated much time to the arrangement of the Osler and to the Rolph collections in its historical section. His life was enriched by many friendships. His personality was genial and his interests many. He was a consistent member of the Anglican Church and was always an exponent of the best ethics of his profession.

He is survived by his widow, a brother and three sisters.

AN APPRECIATION

The long span of years of association and friendship between Norman Gwyn and me began auspiciously back in the Baltimore days, at that far time when Osler presided over medicine in the Johns Hopkins Hospital and Medical School. Norman was a graduate on the staff while I was only a medical student; but there was a common bond—we were both disciples of Dr. Osler.

Then the ways parted. World War I came between but did not wholly dissociate us for both were servants of the King. Norman's excellent service in charge of the medical department of No. 1 Canadian General Hospital in France is a matter of record. In his letters Sir William testified to this good work, mentioning also the casualties and service illnesses the effects of which remained as a handicap throughout his life. Only many years later, after repeated urging, could Norman be persuaded to apply for a pension—which was readily granted together with back pay.

The year 1925 brought us together again, this time in Toronto; and during the years that have passed since we were drawn closer together and our friendship grew deeper and firmer. Indeed friendliness and kindness were dominant in Norman's nature. These qualities were conspicuous in his relations with his older patients—those whom he had cared for over the years and who depended upon him so utterly when sickness came. And he would speak of them not as patients but as old and dear friends, and so they were. They loved him. He was truly a doctor of the old school. Even when gravely ill himself his self-possession and thoughtfulness for others were touchingly in evidence.

One of Norman's most cherished personal associations was his charter membership in the Medical Historical Club of Toronto, dating from 1932—a little group of professional friends who during the winter season meet in their several homes each month for a literary and social evening. Norman's reminiscences and more formal contributions to these evenings were of notable interest and value.

His last public address was given before a special meeting at the Toronto Academy of Medicine, December 9, 1949, to commemorate the 100th anniversary of the birth of Sir William Osler. Norman spoke of Osler's early years and his attitude toward children—how he entertained them, played with them, loved them, made himself one of them. As one listened, Norman might have been recalling his own earlier years for those were his ways with children too, as many grown up children now will doubtless remember.

Altogether the most memorable of my associations with Norman were the many evenings spent at his home. I was taken in as one of the family and our talk ranged far and wide. He was a delightful conversationalist. Recollections would emerge of eminent men with whom he had been associated in various places, especially in Baltimore, Philadelphia, Toronto, and overseas. There were intimate glimpses into the lives and doings of these men, their accomplishments and striking qualities—the kind of men they were.

It was a rare experience to listen to his reminiscences of his uncles, the four great Osler brothers, and sooner or later the talk would be mainly about Sir William. How could it be otherwise? We were of his profession and he was our patron saint. Norman would speak of his later years, the Oxford period, his self-sacrificing war activities and his grievous loss, and then of his own visits to the "Open Arms" at No. 13 Norham Gardens.

Having been a pupil of Dr. Osler, to hear Norman continue the story was next best to listening to Osler himself. For the spirit of Osler lived on in Norman. They were the same breed of men. Theirs was the same sweet, gentle personality. They were animated by the same generous impulses, in friendship a fidelity that was steadfast, come what might, the same rigid code and ethics of the profession, the same consideration for the welfare of their colleagues, their reputation and the integrity of medical practice. But more than all else that intangible something that denotes the manner of the great physician with his patients—that quality of empathy by which he gives something of himself, something that cannot be put in words but which the patient feels and that awakens confidence and hope, aye, and affection, that means so much in contributing to the cure when cure is possible, to mitigating suffering in any case.

Such was the keynote of Osler's nature. It was the keynote of Norman's nature. He was through and through a good man, a fine physician, a staunch friend.

C. B. FARRAR

AN APPRECIATION

For various reasons Norman Gwyn did not bring forth the full fruits of his maturity, and he is probably less well known to the present generation than he deserves. We worked together for nearly two years in No. 1 Canadian General Hospital at Etaples, and it was soon quite obvious to me that he was rather different to the ordinary type of medical officer. The keenness and efficiency of the leading men in that particularly well known hospital were well recognized, but Norman stood out amongst them; not for his military training, for, hating army red tape with all his vigorous soul he had absorbed very little of it; nor yet for his medical qualifications, for high as these were some of Canada's best men were also over there. But he had the quality of being able to withdraw himself, and that is not easy in an active military hospital on active service. His mind was set on clinical medicine, and he made his opportunities for collecting and recording material. This meant hard work, but he had mastered that key to success. And he did his best to inspire others. He even got me to prepare a paper on wounds of the chest, of which of course one could easily assemble many hundreds. He gave new life to a local inter-hospital clinical association, not only contributing but driving others to do so. One always knew instinctively that he was not trying to gain anything for himself, unless it was to satisfy his zeal for medicine. Indeed he would willingly re-write poorly presented material, and still give the credit to the other man. A rare case attracted him like a magnet, and one patient owed him a protracted pleasant convalescence at No. 1 because of a capacity to draw and a willingness to do medical illustrative sketches for Norman. With a little quite reasonable craftiness Norman saw to it that this man was not evacuated to England with any unnecessary haste.

But for all that he was a student, no one had keener social instincts and he was popular in the mess. There may be still some who remember his genial, somewhat

grating chuckle as he officiated at a late party in his hut, and his skill in concocting a Welsh rarebit.

He was good to work for. After all he asked nothing but that one *should* work. That is how I like to think of him—straightforward, enthusiastic, unselfishly solicitous for all that was best in medicine. H.E.M.

DR. JEAN-PAUL HANDFIELD died in Queen Mary Veterans' Hospital, Montreal, on January 20. He was 35. A native of Outremont he received his education at Jean de Breboeuf and Loyola Colleges, McGill University and University of Laval at Quebec. In his graduating year from Laval, 1942, he was student body president. From 1944-46 he served with the R.C.A.M.C. with rank of captain. He took postgraduate courses in Paris in 1950. Dr. Handfield was assistant in medicine at l'Hopital Ste. Jeanne d'Arc and was attached to Queen Mary Veterans' Hospital. Surviving are his widow, two sons and a daughter.

DR. HENRY OLIVER McDIARMID of Brandon died on January 4 at Tampa, Florida, while on holiday. Born in Elmira, Ill., in 1882 he moved to Gladstone at an early age with his family. After graduating from Manitoba Medical College in 1906, he practised at Gladstone then took postgraduate work in ophthalmology at Chicago and New York, then settled at Brandon in 1909. A fine athlete, able speaker and a good citizen he did much for his community and province. He was president of Manitoba Medical Association in 1931-32 and president of the College of Physicians and Surgeons of Manitoba in 1935. He became a charter member when the Royal College of Physicians and Surgeons of Canada was founded in 1937. As a Liberal candidate he contested the seat of Brandon in the provincial legislature but was defeated by Walter Dinsdale. One of his sons, Dr. R. O. McDiarmid of Brandon is a top ranking amateur golfer in Manitoba. In addition to his widow, he is survived by two sons and two daughters.

DR. HERBERT LORNE MINTHORN, aged 69, died on February 10 in Toronto, Ont. Dr. Minthorn, coroner for the Cochrane district for years, had practised medicine in Timmins for 44 years. He had been ill for some time.

Born in Orillia, he was graduated in medicine from the University of Toronto in 1908. Shortly after he established a practice in Timmins and served through the Porcupine area. He was a past president of the Porcupine Medical Society. He is survived by his widow, and a son.

DR. THOMAS FRANCIS MURRAY, aged 59, well-known Calgary doctor and former Indian agent and Medical Superintendent of Sarcee Indian Reservation died February 5 in Holy Cross hospital after a brief illness. Dr. Murray was born in London, Ont., and educated at the London Collegiate Institute and Assumption College at Sandwich, Ont. He received his B.A. and M.D. degrees from the University of Western Ontario in 1919.

During the First Great War he served overseas in France, England and Belgium as a captain and took part in battles at Vimy Ridge, Somme and Passchendaele.

He returned to Canada in 1917 to resume his medical education, and after graduation moved west to Big Valley in 1920. In 1921 he became Indian agent and medical superintendent of Sarcee reservation and held this post until his retirement in 1947 due to ill health. In his work among the Indians, Dr. Murray pioneered the development of T.B. treatment and cut down greatly the death rate from this disease. During the Second Great War, Dr. Murray also took charge of the Morley Indian Reservation. After retirement Dr. Murray took up private practice in Calgary but was forced to retire in 1949 due to ill health. He is survived by his widow and three daughters.

DR. FRANK O'LEARY died of coronary thrombosis on February 3. Born in Orillia in 1891 he was educated in the Separate School and the Collegiate Institute of his native town and graduated from the Ontario College of Pharmacy before entering the study of medicine. As a first year medical student he enlisted with the Canadian Overseas Force and was blown up in a "pill box" at Passchendaele. At the dressing station he was marked "no dressings" but survived with the loss of his left lower limb which was amputated in mid-thigh. He completed his medical course and graduated from the University of Toronto in 1922. After an internship in St. Michael's Hospital he spent two years in the Women's Hospital in New York and then joined the staff of St. Michael's in the Department of Obstetrics and Gynæcology. He succeeded Dr. D'Arcy Frawley as chief of the department and was Associate Professor in the University. Last year he retired under the age limit rule.

Dr. O'Leary was a remarkable man. He had a genius for friendship and a zeal for service that was unique. His knowledge of modern literature was amazing and he was on intimate terms with authors and artists. He contributed to the programs of the Academy and lectured to county medical societies. Few men ever attained such popularity among his colleagues and contemporaries. His zeal and devotion in the social activities of his church and in the military organizations to which he belonged took time and energy. He was Vice-president of the Society for Crippled Civilians and a member of the Board of the War Amputations of Canada and a Captain in the Reserves of the Royal Canadian Artillery. He was President of the Newman Club at the time of his death and was a powerful influence among the students who constitute its membership. It is hard to imagine a life more full of humanitarian effort or a personality more generally beloved by those who knew him. He is survived by his widow, and his infant son Peter.

LE DR. J.-E. NADEAU décédé le 8 janvier à Québec à l'âge de 72 ans et 2 mois.

Pendant 20 ans le Dr Nadeau s'est dévoué au service des immigrés, dans le port de Québec. Il fut à l'emploi du gouvernement fédéral, en cette qualité, de 1904 à 1925. Cette année là, il entra au service du gouvernement provincial en qualité d'assistant du Dr Alphonse Lessard qui dirigeait à ce moment le service de santé du gouvernement.

C'est pendant ce stage du Dr Nadeau au Parlement qu'il fut prêté à la ville de Québec, à la demande de Son Honneur le maire Lucien Borne, pour travailler à la réorganisation du service municipal de santé. A l'hôtel de ville, le Dr Nadeau se dévoua de toutes ses forces pour améliorer les divers services sanitaires puis il céda sa place au Dr Berchmans Paquet qui est le titulaire actuel du département. Le Dr Nadeau fut alors nommé président de la Commission provinciale de l'Industrie laitière, poste qu'il occupa jusqu'en 1950 quand it prit sa retaite.

Le Dr Nadeau laisse dans le deuil son épouse et un fils.

DR. A. D. ROBERTS, formerly of Sault Ste. Marie, Ont., passed away in Toronto, January 11, following a lengthy illness. Born in Newfoundland, Dr. Roberts moved to the Sault in 1930 from New York, to take up medical practice there. He remained in the Sault until 1950 when he moved to Leamington to another practice. In 1951 he became quite ill following three strokes, and was taken to Toronto General Hospital where he died.

He is survived by his widow and three children.

DR. ALEXANDRE RODRIGUE, who was in his 83rd year, died at his home in Lachute, Que., on February 5. Born at Ste. Scholastique, he came to Lachute in his infancy. He first attended the English school here, and later went to Ste. Therese College, where he obtained his B.A. degree. He graduated in medicine from the Montreal Section of Laval University, in 1895.

Starting practice in this town for two years he moved to Buckingham for a period of 10 years, during which time he gained valuable experience as an all-round "country doctor"; he served as district coroner, and

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was active in school and town activities. The next five years were spent at Beauport, Que., but the yearning for his home town brought him back in 1912—since which time he has devoted himself to the care of the sick in Lachute and surrounding districts.

DR. OSWALD E. ROTHWELL, aged 72, prominent Regina neuropsychiatrist and a member of the staff of the Regina General Hospital since 1907, died on January 8 following a long illness. Born in Brantford, Ont., Dr. Rothwell came to Regina in 1892 and attended public school there. He graduated from the University of Manitoba with his Bachelor of Arts degree in 1901 and then attended McGill, where he received his medical degree in 1906.

After being in general practice in Regina for a number of years, he was appointed jail physician in 1912, a position he held for more than 15 years. In 1929 he was appointed first director of the psychiatric wing of the General Hospital, later known as the Munroe wing.

At one time a member of the medical council of Saskatchewan, the executive of the medical council of Canada and a past president of the College of Physicians and Surgeons of Saskatchewan, he was made a life member of the Canadian Medical Association in 1948. Besides his widow, Dr. Rothwell is survived by one son, Dr. William Rothwell, Calgary, and one daughter.

DR. OTTO M. SCHMIDT, McGill graduate and third generation of his family to practise medicine, died in New York City on January 16. He was 54. His father, Dr. A. F. Schmidt, was a well known physician in Montreal and his grandfather, Dr. S. B. Schmidt, served on the faculty of medicine at McGill.

Dr. Otto Schmidt graduated from McGill in 1922 and interned at Royal Victoria Hospital. He left Montreal to become associated with his uncle, Dr. J. E. MacKenty, chief surgeon of the Manhattan Eye, Ear, Nose and Throat Hospital, where he remained. He is survived by his widow and three children.

DR. ARTHUR J. SUTHERLAND, who answered the call of the Klondike and spent most of his life in Alaska, died on January 31 in Honolulu, Hawaii. Dr. Sutherland was born in Toronto 80 years ago and graduated from Trinity College. Following graduation he practised for a time in North Bay, removing a year later to a mining town in the Rocky Mountains. He practised medicine there for some months until the rush of '98 depleted the mine's staff. He answered the call and along with miners followed the trail of '98 northward. On reaching the 30-mile rapids at the northern end of Lake Labarge, like the miners, he built his own raft to take him along the Yukon River to the Klondike area near Dawson City.

DR. THOMAS WALTER SMITH, founder of the Smith Clinic at Hawkesbury, Ont., died recently at the age of 75. Born in Hawkesbury, Dr. Smith graduated in medicine from McGill University in 1902 and practised in his home city for 50 years. He established his own hospital in 1915, which later became the Smith Clinic, now under the direction of his two sons,

A Fellow of the American College of Surgeons, he was a charter member and past president of the Rotary Club of Hawkesbury, and an outstanding breeder of thoroughbred Ayrshires. He is survived by his widow and two daughters.

DR. FREDERICK H. WILSON, recently appointed Medical Officer of Health for Kent County, Ont., died of a heart attack on January 23. He came to the county in late December and assumed his duties at the beginning of January. Dr. Wilson formerly resided in Shelburne, Ontario, where for five and a half years he was M.O.H. for Dufferin County and head of the health department there. Prior to that he was engaged as a general practitioner in Englehart in Northern Ontario where he was M.O.H. for the town and surrounding townships. A former surgeon lieutenant-commander in the R.C.N. he leaves a widow and two sons.

ABSTRACTS *from current literature*

MEDICINE

Major Surgery in Patients with Healed Myocardial Infarction.

HANNIGAN, C. A., WROBLEWSKI, F., LEWIS, W. H. JR. AND LADUE, J. S.: AM. J. M. SC., 222: 628, 1951.

In an attempt to assess more correctly the influence of a past history of coronary thrombosis, recent or remote, on the mortality of subsequent major surgical procedure, these authors studied 58 cases in whom this cardiac complaint had occurred and in whom necessary operations for malignant growths were later performed. There was an overall mortality of 5.2% which, in comparison with a similar "normal" group of patients exposed to an equally wide range of operations in whom the rate was 3.4%, they consider not to be excessive. Four patients had fresh infarctions, four had bronchopneumonia, five had congestive failure, one had a pulmonary embolis, three patients died with shock.

A waiting period of six weeks at least after the acute myocardial infarction is advised. They found that there was quite a sharp rise with increased lengths of operation time. Pentothal seemed to be associated with a significantly greater incidence of complications than did ether, spinal anæsthesia or local anæsthesia. The incidence of complications was apparently more related to cardiac enlargement than to such factors as sex, age of infarct, angina or hypertension. The final conclusion is that if adequate care is taken the history of past coronary thrombosis need not be a complete deterrent to major surgical procedures in the future.

G. A. COPPING

Prolonged Uninterrupted Cortisone Therapy in Rheumatoid Arthritis.

BOLAND, E. W.: BRIT. M. J., 2: 191, 1951.

Thirty-six women and twenty-four men with rheumatoid arthritis were treated with cortisone for six to fifteen months. There was very marked improvement in 30%, marked in 50%, moderate in 18%, and slight in 2%. Women are more likely to develop side reactions than men, 44% of the women and 29% of the men exhibited reactions. The severity of the reaction varied directly with the size of the dose of cortisone.

Mooning of the face occurred in 20% of the patients: this was due to fat deposition in the cheeks and varied in extent with the size of the dose of cortisone. Glycosuria occurred in 0.5% of the series treated, it was easily controlled by dietary restrictions. Protein catabolism is increased by cortisone therapy causing an elevation of the urinary nitrogen. Electrolyte metabolism was altered in the patients receiving more than 75 mgm. cortisone per day, œdema indicated sodium and water retention. This œdema cleared up by lowering the daily dose of cortisone, and restricting salt in the diet. Hypertrichosis occurred in 1.1% of the women, and acneiform eruptions occurred in 0.5% of the total series. Three women had oligomenorrhœa and two had spontaneous fractures due to osteoporosis from excessive calcium mobilization and excretion. Psychomotor activity was markedly increased with the initial doses of cortisone and lessened as the maintenance dosage was established. Adrenal cortical function was depressed by cortisone administration but was restored to normal following cessation of therapy in ten to ninety days.

J. A. STEWART DORRANCE

The Newer Knowledge of Atherosclerosis.

FIRSTBROOK, J. B.: BRIT. M. J., 2: 133, 1951.

A study of medical statistics, 1940-45 for Sweden and the U.S.A. showed a marked correlation for the occurrence of atherosclerosis with a consumption of food of

high cholesterol content. Etiological factors are varied; it is a slowly developing condition, hence it is more frequently found in the older age groups; hypercholesterolæmia is known to be an important factor and all incidences of experimental atherosclerosis have been induced by the administration of cholesterol, and all atherosclerotic lesions have a high content of cholesterol; obesity is very frequently associated with atherosclerosis and statistics show that lean individuals are less prone to atherosclerosis. Experimentally induced atherosclerosis does not always show a definite relationship between the degree of involvement and the level of cholesterol in the diet, nor is there a relationship between blood-cholesterol levels and atherosclerosis. Hypertension is definitely associated with atherosclerosis, it occurs twice as frequently in hypertensives as in normotensives and hypotensives. Arterial damage predisposes to the deposition of cholesterol at the site of damage. The rate of development is in many instances dependent upon the blood pressure. There is considerable evidence that the correction or prevention of obesity will prevent atherosclerosis, and a diet of low animal fat (*i.e.*, low in cholesterol) will be of additional help.

J. A. STEWART DORRANCE

Treatment of Acute Thyroiditis with Anti-Thyroid Drugs.

REVENO, W. S. AND ROSENBAUM, H.: NEW ENGLAND J. MED., 245: 364, 1951.

Acute thyroiditis generally occurs in middle-aged women with or without goitre and with or without an antecedent history of infection (usually respiratory). The onset is usually vague with low-grade fever, malaise, and pains about the neck, jaw and ears. The pain gradually localizes to the thyroid which becomes swollen and tender, with tenderness on extension of the head and dysphagia. Hyperthyroid symptoms often develop but, in general, spontaneous resolution occurs without any residual thyroid dysfunction.

Operation is rarely indicated in treatment. X-ray therapy, while helpful, carries with it the risk of subsequent myxœdema. Iodine, heat, cold and the antibiotics exert no favourable influence.

Three cases are reported where anti-thyroid drugs (thiouracil in one and tapazol in two) appeared to have therapeutic benefit. It is noteworthy that in one of these cases of acute thyroiditis myxœdema became evident three months after the subsidence of the acute process.

NORMAN S. SKINNER

Metabolic Effects of the Rice Diet in the Treatment of Hypertension.

CURRENS, J. H., REID, E. A. S., MACLACHLAN, E. A. AND SIMEONE, F. A.: NEW ENGLAND J. MED., 245: 354, 1951.

The effect of the rice and fruit diet of Kempner was carefully studied on a small group of seven patients with hypertension. In only two cases was there a significant lowering of blood pressure which was raised in one patient by the administration of sodium chloride, suggesting that the low sodium content of the diet was its significant feature. A definite lowering of the basal metabolic rate, with a slower fall in blood cholesterol, was apparently not due to thyroid suppression since there were no changes in the protein-bound serum iodine. An initial negative nitrogen balance, accompanied by weight loss, diminished progressively and almost stabilized after two to three months on the diet. Decreased renal clearances were demonstrated and were considered due to the low-protein content of the diet.

NORMAN S. SKINNER

Urinary and Fæcal Excretion of Mercury in Man Following Administration of Mercurial Diuretics.

GROSSMAN, J. E. *et al.*: J. CLIN. INVESTIGATION, 30: 1208, 1951.

Following intravenous or subcutaneous injection of 2.0 ml. of Thiomerin intramuscular injection of 2.0 ml. of Mercuhydrin 60 to 95% of the injected mercury is excreted in the urine in 24 hours. It continues to be excreted in the urine for 48 to 72 hours or longer, in varying amounts. Fæcal excretion rarely exceeds 1 to 2 mgm. per day. Within 2½ to 3 hours about 50% of the mercury is excreted in the urine after intravenous injection, while after subcutaneous injection the rate of excretion during the first 30 to 60 minutes is reduced. All the administered mercury may be found in the fæces and urine when the analysis is continued for some length of time. Ammonium chloride, which enhances, and desoxycorticone acetate, which inhibits, the diuretic response, have no effect on the total excretion of mercury. Aminophylline accelerates urinary mercury excretion, maximum effects within ½ hour when the mercury excretion rate is nearly doubled, followed by a relative slow excretion of mercury.

J. A. STEWART DORRANCE

SURGERY

Subtotal Adrenalectomy for Cushing's Syndrome.

PRIESTLEY, J. T., SPRAGUE, R. G., WALTERS, W. SALASSA, R. M.: ANN. SURG., 134: 464, 1951.

Cushing's syndrome is characterized by several clinical features: an abnormal obesity and wasting of muscle with a big trunk and thin extremities, hypertension, osteoporosis, ecchymosis, diabetes, amenorrhœa or impotence, hirsutism and acne. Varied endocrine pathologic changes are noted: thymic tumour, basophile cell changes in the anterior pituitary and tumours of the adrenal cortex. ACTH and cortisone in large doses cause similar pituitary changes. It seemed that removal of sufficient adrenal cortical tissue should lessen the symptoms of Cushing's syndrome.

This is a report of the effect of radical subtotal adrenalectomy on 29 patients at the Mayo Clinic. ACTH or cortisone was used in the preoperative and postoperative care and in the treatment of the usual severe delayed reaction. The surgical management and results are described. There were 6 deaths and 19 had an "excellent remission" of the Cushing's syndrome.

BURNS PLEWES

Endometriosis of the Vermiform Appendix. Review of the Literature, with the Addition of Nine New Instances.

COLLINS, D. C.: ARCH. SURG., 63: 617, 1951.

Endometriosis of the appendix veriformis, though of rather rare occurrence, is more frequently recognized since the pathologist and the surgeon have learned to identify its gross and microscopical characteristics. The author reviews the various theories of the etiology of endometriosis and presents related facts of embryology and of pathology. Each endometrial lesion is in reality a miniature uterus with functioning glands and usually stroma. Collins summarizes in a table the data reported in the literature on endometriosis of the vermiform appendix, as presented by 64 authors between the years 1860 and 1951.

He reports nine proved instances of this lesion, including one with severe rectal bleeding and marked secondary anæmia. Following an appendectomy the patient has remained well. With the addition of these nine cases the total number reported in the literature is now 134.

G. E. LEARMONTH

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Thyroiditis.

SCHLICKE, C. P.: ARCH. SURG., 63: 656, 1951.

There is little that is known about thyroiditis and seldom is this disease recognized. The better known types are the ligneous thyroiditis, described by Riedel in 1896 and the stroma lymphomatosa described by Hashimoto in 1912.

As Schlicke remarks, "the various forms of thyroiditis are a strange group of diseases. The etiology is unknown. The terminology and classification are confused and concepts of pathogenesis are in controversy. Women are afflicted far more often than men." He classifies the various types as acute, subacute and chronic. In this article he deals only with subacute and chronic thyroiditis and of these forms presents 13 cases. Of these seven were of the subacute type and were treated by thiourates, x-rays and antibiotics. Six patients had chronic thyroiditis and included two with Hashimito's disease, two with Riedel's struma, while two were unclassified. Subtotal thyroidectomy was performed in all of the six patients, with recovery in each instance. G. E. LEARMONTH

The Surgical Treatment of Ventricular Fibrillation.

JOHNSON, J. AND KIRBY, C. K.: ANN. SURG., 134: 672, 1951.

Ventricular fibrillation may be caused by manipulation of the heart, contact with its conduction mechanism or anoxia. Coronary artery disease and cyclopropane may predispose. Intrapericardial procaine is used to prevent fibrillation. During the past 10 years defibrillation has been attempted in 10 patients and in four there was complete recovery. In 7 patients there was complete cardiac arrest and ventricular fibrillation began after cardiac massage for several minutes.

The measures for achieving success are described. Adequate circulation by cardiac massage and artificial ventilation of the lungs must be established within four minutes. If it takes longer the patient will be decerebrate even if regular beat is restored. Once cardiac massage and oxygenation is achieved, haste is not vital. A rapid intravenous should be started, procaine or pronestyl administered, and defibrillation achieved by electric shock. The electric defibrillation is described and it is evident that the shock must be a powerful one for the patient's whole body is thrown into violent contractions with each stimulation.

Two cases are described in which patients who were undergoing cardiac catheterization, went into ventricular fibrillation a block from an operating room and recovered completely after heroic sprinting, cardiac massage, mouth-to-mouth respiration and defibrillation.

BURNS PLEWES

GYNÆCOLOGY AND OBSTETRICS

Iron Metabolism in Pregnancy.

KLOPPER, A. AND VENTURA, S.: BRIT. M. J., 2: 1251, 1951.

In late pregnancy iron deficiency states are difficult to assess by ordinary hæmatological investigations. The levels of serum iron, the iron-binding capacity of the serum proteins, the serum copper, and the protoporphyrin were investigated in normochromic anæmia and in hypochromic anæmia. In true iron deficiency states these show a characteristic pattern which is quite different from the normal. This characteristic pattern was outlined in nine cases of microcytic hypochromic anæmia, and the regeneration towards normal was studied when these cases were given intravenous iron.

ROSS MITCHELL

Toxæmia of Pregnancy.

BUCHAN, T. W.: BRIT. M. J., 2: 1011, 1951.

In view of the possible relationship between eclampsia and both acute nephritis and rheumatic fever, the regional distribution in England and Wales of mortality from these diseases and from scarlet fever, puerperal fever and stillbirth is considered.

Eclampsia and stillbirth have a similar regional distribution and are in frequent association clinically.

A close correspondence exists between the regional variations of mortality from eclampsia, from nephritis and from puerperal sepsis, a circumstance which, along with the other relationships indicated, would seem to support the use of cortisone in toxæmia of pregnancy, as well as in other diseases suspected of being streptococcal allergic disorders. ROSS MITCHELL

Ovarian Pregnancy.

GÉRIN-LAJOIE, L.: AM. J. OBST. AND GYNEC., 62: 920, 1951.

Outmoded methods by gross examination of specimens of presumably ovarian pregnancies should be discarded. Histological findings are insufficient to prove the origin of an ovarian pregnancy. Close co-operation of the pathologist and gynæcologist is indispensable to the solution of this difficult problem. Two cases are reported to demonstrate these contentions. ROSS MITCHELL

The Malignancy of Special Ovarian Tumours.

HENDERSON, D. N.: AM. J. OBST. AND GYNEC., 62: 816, 1951.

The possibility of recurrence of the granulosa-cells, carcinoma and the dysgerminoma is sufficiently great to warrant bilateral oöphorectomy and hysterectomy for these neoplasms. A known recurrence rate for the arrhenoblastoma warrants consideration of radical surgery for this rare type of ovarian tumour. ROSS MITCHELL

PÆDIATRICS

Exchange Transfusion for Fetal Erythroblastosis.

KAESSLER, H. W. AND LEGARD, J. J.: J. PEDIAT., 39: 174, 1951.

Indications for exchange transfusions are: during pregnancy—Rh (d) negative mother with Rh (D) positive father, positive indirect Coombs test, increasing titre of Coombs test, history of previous sensitizations, and history of previous administration of sensitizing blood; at delivery, icteric amniotic fluid, large pale placenta, icterus of infant, pallor, hæmorrhagic manifestations, œdema, hepatosplenomegaly, anæmia of less than 15 gm. per 100 ml. blood, positive Direct Coombs test, and erythroblastosis; during neonatal period—increasing icterus, fall of hæmoglobin and erythrocytes, toxicity and hæmorrhagic tendencies. The infant should be given freshly drawn blood of the same group and Rh (d) negative, given in 10 ml. aliquots to 500 ml., with the withdrawal of 450 ml., in 9 ml. aliquots to give a positive balance. The umbilical vein route may be used during the first 24 hours of life, thereafter a saphenous vein cut-down should be used with the insertion of a fine plastic tube. Tetany due to sodium citrate in the donor blood may be controlled with 1 ml. of 10% calcium gluconate for every 70 to 100 ml. of donor blood. The apparatus should be rinsed with a heparin-saline solution (1,000 units/100 ml. saline) about every 10 strokes of the injecting syringe to prevent sticking. As a prophylactic measure an antibiotic may be given.

J. A. STEWART DORRANCE

Management of Anæmia in Childhood.

PIERCE, M. I.: POSTGRAD. MED., 11: 68, 1952.

Anæmia in childhood may be due to many etiological factors: maternal and fetal relationships affecting fetal blood destruction and formation; the rate of growth in infancy and early childhood; the repeated infections of childhood interfering with the utilization of iron, vitamins, and food; and the hereditary factors which determine the severe constitutional anæmias. Hæmolytic disease of the newborn (erythroblastosis fetalis) develops in the first few hours or days of life. The Rh antibodies are more damaging than the AB antibodies and cause more severe degrees of anæmia. Kernicterus, with its sequelæ of brain damage, is more commonly the result of Rh incompatibility. Small multiple transfusions or replacement transfusions lower the mortality rate. The standard type of small transfusion repeated when necessary is preferable to the replacement type unless an experienced operator is available. Nutritional anæmias of infancy are iron deficiency anæmias due to: presence or absence of anæmia in the mother; the period of gestation; infant size at birth; rapid increase in body weight; the supply of iron in the infant's diet; absorption of iron; and infection. This may be corrected by increasing the foods rich in iron in the diet, or by supplementing with ferrous sulphate, the administration of liver and liver concentrates and vitamin B_{12}. Megaloblastic anæmia is a nutritional anæmia in infancy and responds promptly to the oral administration of folic acid, 15 mgm., and ascorbic acid, 100 mgm., daily. Anæmia of infection occurs in older children more frequently than does nutritional anæmia and iron absorption is reduced while iron is bound to the inflamed tissue and is not available for synthesis into hæmoglobin. Iron supplements are of benefit in this anæmia. Hæmolytic anæmia may be due to the toxicity of infections or it may be familial or racial in origin. The first type responds to ACTH although the mechanism of action here is unknown. Familial and racial types (congenital hæmolytic anæmia, Mediterranean anæmia, or thalassæmia and sickle cell anæmia) respond poorly to therapy, although splenectomy may be of some help in prolonging life, but few children survive beyond early childhood. Aplastic and hypoplastic anæmias, are either idiopathic or secondary to noxious agents, and respond favourably to repeated transfusions. The management of anæmias in childhood requires knowledge of the underlying etiology with definite indications for the use of iron, vitamin B_{12}, and liver as well as transfusions.

J. A. STEWART DORRANCE

DERMATOLOGY

Clinical, Social and Occupational Aspects of Industrial Dermatitis.

HEWITT, M.: LANCET, 261: 1105, 1951.

This paper is of more than passing interest in the literature dealing with the subject of industrial dermatitis. Estimates of the incidence of industrial dermatitis expressed as a percentage of all cutaneous disorders vary greatly, the range being from 0.04% (Crocker, 1903) and 20% (Hazen, 1914) up to 66% (Sequeira, Ingram and Brain, 1947). The author ascribes this wide discrepancy to a lack of unanimity as to what constitutes industrial dermatitis. No difficulty arises in certain well-recognized clinico-pathological entities such as pitch-cancer, chloracne or chrome ulceration, but the majority of cases labelled industrial dermatitis are simply dermatitis arising during employment involving contact with dusts, liquids and vapours. There is hardly any substance encountered at work or in leisure which cannot produce sensitization, yet in patch-testing 1,000 persons with paraphenylenediamine Ingram (1932) found only 4% naturally sensitive to the substance. The idea that any eruption occurring during employment is most likely to have been produced by an external irritant encountered there prevails widely, however, not only among the laity but in the medical profession as well.

The author made a study of 80 consecutive cases of industrial dermatitis of over two months' duration and found that unsatisfactory work records and severe social and emotional difficulties were so conspicuous in the series that it was concluded that these factors were an integral part if not a cause of the malady. It was found that due to persistence of skin disorders throughout a number of changes of occupation which the subject in many cases had tried it was impossible to classify the cases according to occupation, and that more light seemed to have been shed by analysis of social and work records. Support was furnished for MacCormac's suggestion that "idiopathic eczema" and industrial dermatitis may be the same disease. The presence of atopic eczema and seborrhœic dermatitis was observed in many subjects. The prevalence of belief in and fear of industrial dermatitis is wide. The dangers of injudicious use of strong antiseptics by nurse and first-aid workers (*detergents also* —Abst.), the frequent ineffectiveness of improved hygienic environment, barrier creams, etc., and the necessity of a more enlightened joint clinical, social and occupational approach are well emphasized. This paper should be required reading for all whose practice includes dealing with dermatitis in industrial workers.

D. E. H. CLEVELAND

Microsporosis of the Scalp. Evaluation of a New Therapeutic Agent.

APPEL, B., TYE, M. J., HALPERN, W. AND PACI, D.: NEW ENGLAND J. MED., 245: 1003, 1951.

This report from the Department of Diseases of the Skin at Tufts College Medical School is on laboratory and clinical tests of a new antifungoid preparation at present marketed as Asterol Dihydrochloride. Nine children from a large group diagnosed as having microsporosis capitis ("ringworm of the scalp") furnished hairs which fluoresced under Wood's light. These hairs were exposed to either 2% tincture or a 2% water-soluble ointment of the substance. Growth of both *M. canis* and *M. Audouini* was inhibited in 48 hours by the tincture but after 14 days' exposure to the ointment one culture of *M. canis* and two of *M. Audouini* continued to grow. Neither the tincture or the ointment was 100% successful in suppressing viability. 61 children were treated, of whom 31 were treated for less than 3 months. None of those treated for less than 3 months was cured. Of 30 children treated for more than 3 months 5 out of 6 cases with *M. canis* were cured, but only 5 out of 24 with *M. Audouini* were cured. Other observers have reported better clinical results with concentrations up to 5%, with no primary irritation or sensitization. They do report however that 10% is a primary irritant. The authors encountered neither primary irritation or sensitivity with 2%, but recommend that further trials with bigger concentrations should be done, and believe that the drug merits further consideration. D. E. H. CLEVELAND

ACTH and Cortisone in Diseases of the Skin.

LEVER, W. F.: NEW ENGLAND J. MED., 245: 359, 1951.

This study reflects the experience in the use of ACTH or cortisone in a group of over 70 cases of skin disease. These hormones are considered to be of considerable value in the treatment of pemphigus, systemic lupus erythematosis. dermatomyositis and generalized exfoliative dermatitis. In chronic, inflammatory nonfatal dermatoses ACTH and cortisone should be only used in patients who are so ill that they are bedridden, since results are only temporary and treatment must be continued for a long time.

In atopic eczema, psoriasis and chronic discoid lupus erythematosis temporary improvement may result from

the use of ACTH or cortisone but there is a strong tendency for the disease to flare up in an exaggerated form when therapy is discontinued.

NORMAN S. SKINNER

INDUSTRIAL MEDICINE

Employment of the Older Worker.

KLUMPP, T. G.: CONNECTICUT HEALTH BULL., 65: 247, 1951.

That the age shift in population, with the older persons rapidly increasing in number and at the same time being healthier than they used to be, is very significant in relation to the entire economic and political structure of the nation, is becoming recognized. In this article which was one of the papers given at the Connecticut Conference on Chronic Disease in May, 1951, the author stresses the contribution which the partially disabled and the elderly workers can make to the defence effort. Their employment and continued employment beyond present-day standards is of utmost importance to our future economy. He discusses the situation from two distinct points of view—from the standpoint of the needs and wants of older people, the "human side", and from the standpoint of the economics of the problem, the "economic side".

Employment is essential to human happiness. Age demands useful work. Society has been quite illogical and inconsistent in its attitude towards the older worker as far as compulsory retirement is concerned. In government, business and the professions, individuals in the older age groups are holding many top and critical positions; for the rank and file of workers there are blind and unselective compulsory retirement rules which automatically eliminate those who have reached the same age, regardless of their fitness-ability and contribution to the group for which they labour. The view that older individuals become over-conservative is disproved by the achievements of many well-known persons. Examples are given.

From an economic standpoint, older workers should be permitted to continue working as long as they are productive and desire to work. Productivity is important to national economy and a large working population is essential to productivity. When large numbers of the population are unemployed, the economic turnover is at a low level. If present-day working standards and conditions are allowed to continue the country may soon be confronted with a large potential labour surplus. Development of new industries will lead to increased employment but on the other hand consideration must be given to the accomplishments of science which are providing the pattern of a great socio-economic revolution. The labour-saving devices may promote the possibility of many additional unemployed. It must be remembered that someone has to support those who are retired to idleness. If the country could employ some of those who are over 65 years of age, it would ease the financial burden of younger workers—either taxes or direct contributions.

In conclusion he states "The fixed formula of retirement must be made more flexible and broken down into several alternative possibilities permitting those fully productive to continue working at their jobs, job reassignments for those fit for other duties, down-grading and 'tapering off' where necessary, and retirement for those who seek it or have been found unsuitable for any work whatsoever." MARGARET H. WILTON

Injuries to the Head: Psychiatric Implications in Their Management.

GARNER, H. H.: INDUST. MED., 20: 507, 1951.

Increasing industrialization coupled with an increase in mechanization of travel has resulted in the problem of head injuries assuming a position of major importance in our society. Their significance from a personal, an industrial and a social viewpoint has seldom been fully understood. The author of this article presents his views as to the nature of these injuries and the importance of proper management. In dealing with head injuries the psychological viewpoint must be taken into consideration. Injury to the brain is the significant factor; where this has not occurred, organic disability should be minimal. The author discusses the factors which contribute to the development of traumatic neuroses in industry as these may result from an injury to the head or to any part of the body. Of particular significance are the following: Each individual has a limited adaptability to withstand stress; injury to other workers continuously acts as a stress to those who were uninjured; anticipation of an injury against which, one is helpless, makes the individual excited. It must be remembered too that individuals with a limited capacity to choose new work or new occupations are likely to be incapacitated by phobic reactions to the work situation in which they were injured. The awareness of hazards involved in any occupation tends to keep the nervous system in a state of tension.

The medical management of head injuries is very important. Much can be done in the prevention of traumatic neuroses by a wise patient-physician relationship. In the period immediately following the accident the industrial physician should try to create an atmosphere of assurance and rest. Careful questioning about the incidents occurring at the time of the accident will help to clear up amnesic reactions which may become dissociated; questions about the injury itself must also be carefully worded to avoid having psychonoxious effects. Should symptoms become somewhat fixed by time, the patient may require the help of a psychiatrist. At all times the phobic reactions of the individual should be sufficiently respected so that an employee is not constantly urged to return to a position he can no longer face without anxiety. MARGARET H. WILTON

FORTHCOMING MEETINGS

CANADA

QUEBEC DIVISION, C.M.A., Annual Meeting, North Hatley, Que. (Dr. G. W. Halpenny, Secretary, 1538 Sherbrooke St. W., Montreal.) May 2-3, 1952.

AMERICAN COLLEGE OF SURGEONS, Sectional Meeting, Royal York Hotel, Toronto, Ont. (Dr. H. P. Saunders, 40 E. Erie St., Chicago 11, Ill.) May 15-17, 1952.

CANADIAN SOCIETY OF MICROBIOLOGISTS, University of Montreal, Montreal, Quebec. (Dr. N. E. Gibbons, Secretary-Treasurer, Division of Applied Biology, National Research Council, Ottawa 2, Ont.) June 5-7, 1952.

CANADIAN MEDICAL ASSOCIATION, Annual Meeting, Banff Springs Hotel, Banff, Alberta. (Dr. T. G. Routley, 135 St. Clair Ave., West, Toronto 5, Ont.) June 9-13, 1952.

SOCIETY OF OBSTETRICIANS AND GYNÆCOLOGISTS OF CANADA, Annual Meeting, Banff Springs Hotel, Banff, Alberta. (Dr. G. A. Simpson, Secretary, Royal Victoria Hospital, Montreal, Que.) June 6-8, 1952.

CANADIAN PUBLIC HEALTH ASSOCIATION, Annual Convention, Fort Garry Hotel, Winnipeg, Man. (Canadian Public Health Association, 150 College St., Toronto 5, Ont.) June 15-18, 1952.

UNITED STATES

AMERICAN CONGRESS ON OBSTETRICS AND GYNÆCOLOGY, 5th Congress, Netherland Plaza Hotel, Cincinnati, Ohio. (Mr. Donald F. Richardson, Executive Secretary, American Committee on Maternal Welfare, 116 South Michigan, Chicago 3, Ill.) March 31 to April 4, 1952.

AMERICAN GOITRE ASSOCIATION, Annual Meeting, St. Louis, Missouri, May 1-3, 1952.

AMERICAN ASSOCIATION FOR THORACIC SURGERY, Baker Hotel, Dallas, Texas, May 8-10, 1952.

AMERICAN ELECTROENCEPHELOGRAPHIC SOCIETY, 6th Annual Meeting, The Hotel Claridge, Atlantic City, N.J. (Dr. John A. Abbott, Secretary, Massachusetts General Hospital, Boston 14, Mass.) May 10-11, 1952.

NATIONAL TUBERCULOSIS ASSOCIATION AND ITS MEDICAL SECTION, The American Trudeau Society, Annual Meeting, Statler Hotel, Boston, Mass. (Dr. H. L. Mantz, 1103 Grand Ave., Kansas City, Mo.) May 26-29, 1952.

AMERICAN COLLEGE OF CHEST PHYSICIANS, 18th Annual Meeting, Congress Hotel, Chicago, Ill. (Executive Offices, American College of Chest Physicians, 112 E. Chestnut St., Chicago 11, Ill.) June 5-8, 1952.

AMERICAN MEDICAL ASSOCIATION, Annual Session, Chicago, Ill. (Dr. George F. Lull, 535 N. Dearborn St., Chicago 10, Ill.) June 9-13, 1952.

AMERICAN UROLOGICAL ASSOCIATION, Annual Meeting, Chalfonte-Haddon Hall, Atlantic City, N.J. (Dr. Charles H. DeT. Shivers, Boardwalk, National Arcade Bldg., Atlantic City.) June 23-28, 1952.

AMERICAN CONGRESS OF PHYSICAL MEDICINE, 30th Annual Scientific and Clinical Session, The Roosevelt Hotel, New York, N.Y. (Dr. Walter J. Zeiter, Executive Director, Am. Congress of Physical Medicine, 30 N. Michigan Ave., Chicago 2, Ill.) August 25-29, 1952.

CONGRESS OF ANÆSTHETISTS, THE INTERNATIONAL ANÆSTHESIA RESEARCH SOCIETY AND THE INTERNATIONAL COLLEGE OF ANÆSTHETISTS, 27th Congress, Cavalier Hotel, Virginia Beach, Va. (Laurette McMechan, Executive Secretary, 318 Hotel Westlake, Rocky River, Ohio.) September 22-25, 1952.

OTHER COUNTRIES

INTERNATIONAL COLLEGE OF SURGEONS, Madrid, Spain. (Dr. Max Thorek, 850 West Irving Park Road, Chicago, Ill.) May 20-24, 1952.

CONGRESS ON DIABETES MELLITUS, The International Diabetes Federation, Leyden, Netherlands. (Dr. F. Gerritzen, 33 Prinsegracht, The Hague, Netherlands.) July 7-12, 1952.

BRITISH CONGRESS OF OBSTETRICS AND GYNÆCOLOGY, 13th Congress, Ripley Smith Hall, University of Leeds, Leeds, England (Dr. B. Jeaffreson, The Hospital for Women, Coventry Place, Leeds, Yorkshire.) July 8-11, 1952.

COMMONWEALTH AND EMPIRE HEALTH AND TUBERCULOSIS CONFERENCE, 3rd Conference, Central Hall, London, England. (Secretary General, National Association for the Prevention of Tuberculosis, Tavistock House North, Tavistock Square, London, W.C.1) July 8-13, 1952.

INTERNATIONAL CONGRESS OF RADIOLOGY, 7th Congress, Copenhagen, Denmark, July 14-19, 1952.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, London, England. (Dr. A. C. Boyle, 45 Lincoln's Inn Fields, London, W.C.2) July 14-19, 1952.

INTERNATIONAL CONGRESS OF DERMATOLOGY, 10th Congress, London, England. (Dr. G. B. Mitchell-Heggs, St. Johns Hospital, Lisle St., Leicester Square, London, W.C.2) July 21-26, 1952.

INTERNATIONAL UNION AGAINST TUBERCULOSIS, 12th Congress and the International Congress on Diseases of the Chest, 2nd Congress, sponsored by the Council on International Affairs of the American College of Chest Physicians, Rio de Janeiro, Brazil. (Executive Officer, American College of Chest Physicians, 112 E. Chestnut St., Chicago 11, Ill.) August 24-30, 1952.

INTERNATIONAL CONGRESS ON NEUROPATHOLOGY, Rome, Italy (Dr. C. M. Fisher, The Montreal General Hospital, 66 Dorchester St. E., Montreal, Que.) September 8-13, 1952.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Friends House, London, N.W.1, England. (Sir Harold Boldero, 12 Pall Mall East, London, S.W.1) September 15-18, 1952.

NEURORADIOLOGIC SYMPOSIUM, Stockholm, Sweden (Docent Ake Lindborn, Serafimerlasarettet, Stockholm K, Sweden.) September 17-20, 1952.

NEWS ITEMS

BRITISH COLUMBIA

There has been considerable interest in British Columbia lately, and especially in Vancouver, in the question of "fluoridation" of the water supply. The proponents of the plan, which has been strongly urged on the City Council, claim that it will secure a great improvement in the teeth of children, where fluorine is added in this way. The B.C. Dental Association, the Vancouver Dental Society, and the City's Medical Health Officer, Dr. Stewart Murray, with others, have strongly supported the plan, and there would appear to be considerable evidence in its favour. The City Council has, temporarily at least, turned it down. From the point of view of the casual onlooker there are some objections, for whatever they are worth. One hears that it has been tried in various areas, and discarded after some years of use, that it has certain undesirable side-effects, especially in adults, and so on.

Since the outstanding causes of dental caries in children are left operating, such as the excessive use of sweets and soft drinks, one hesitates rather to go overboard in support of a scheme such as this, but, on the other hand, it is difficult to withstand the large body of opinion in its favour.

The B.C. Health Department's Tuberculosis Division is urging wider use of B.C.G. vaccine throughout the province as a protective measure.

Dr. G. F. Kincade, Director of T.B. Control, is reported to have made several very striking statements in this regard. First, that it has practically eliminated tuberculosis as an "occupational hazard" for nurses in hospitals, hospital employees and the like. All student nurses in Vancouver and Victoria are given the vaccine, and it has almost completely prevented the incidence of the disease in this group.

The experience of other countries with this vaccine, notably in Europe, and in British Columbia, has been so uniformly favourable that the Department feels that all who have come into contact with T.B. should be vaccinated. The vaccine is available in all health units, and will be supplied to doctors for their use.

A "Conquer Cancer" campaign will be launched in B.C. in April. The objective will be $250,000, of which $100,000 will be given to the Cancer Foundation, whose new building in Vancouver is nearing completion, for furnishings and equipment—while $150,000 will go to the maintenance of the program of the B.C. Cancer Society. Mr. Hubert Wallace is the Campaign Chairman.

Dr. Wallace Wilson, former President of the Canadian Medical Association, and well known to all Canadian medical men, has been elected President of the Vancouver Community Chest and Council for 1952, succeeding Mrs. Gordon Selman. Dr. Wilson has for years been an ardent worker in community chest work, especially in the matter of the care of the aged.

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Dr. E. C. McCoy of Vancouver has been elected Chairman of the Board of Directors of the Medical Services Association of B.C. for 1952. He is the first man to assume this position. He has been a member of the Board as a representative of the medical profession, and has earned the confidence and respect both of his profession and of the Board.

The recent death of Dr. William C. McKechnie of Vancouver at the age of 77, has removed one of Vancouver's leading general practitioners. He had a very high reputation as an obstetrician, and was an extremely skilful and competent surgeon. He also carried on a large general practice, till ill-health forced his retirement some years ago.

Dr. McKechnie was a brother of the late Dr. R. E. McKechnie, former president of the Canadian Medical Association, and Chancellor of the University of British Columbia. His son is Dr. Robt. E. McKechnie of Vancouver.

Dr. McKechnie had many interests other than his profession. He was a very ardent naturalist, and helped found a society in B.C. along these lines. He was keenly interested in botany and photography. A quiet, rather retiring man, he lived a very full and most useful life.

The recent split in the Coalition Government of British Columbia has somewhat stalled developments in the matter of the B.C. Hospital Insurance Scheme. Last year, as we have previously recorded, the Legislature appointed a special Committee to consider the whole scheme, and report on it with recommendations. This Committee, which was non-partisan, and included the Leader of the Opposition, the Hon. R. L. Winch, spent many months and did a most thorough job of investigation, covering every part of the Province, and visiting other provinces. Their report is now complete, and has, we believe, been handed in, but the Premier, Hon. Byron Johnson, and his followers in the House, have decided that this is too important a matter to be settled at a Session where the Government is itself split asunder, and though several members, and especially Mr. Winch, feel strongly that the public is entitled to a clearing up of this very troubled question, it is clear that nothing will be done till after the next election, which will be held, it is stated, very soon.

In connection with this matter, an incident which occurred a few days ago in Victoria has its amusing side, especially as all turned out well. In a car collision several persons received minor injuries. One of them, the only one, we believe, who would have been better for hospital care, was entirely unable to obtain a bed in any hospital in Victoria, or so the papers reported. He had to be confined to his room in the Empress Hotel, with a nurse in attendance. He happened to be the Hon. Sydney Smith, M.L.A., the Chairman of the Legislative Committee appointed to examine into the workings of the B.C.H.I.S., the Committee to which we referred above. He at least will be inclined to agree with what the doctors of B.C. have been saying right along, that there is a grave shortage of hospital beds in British Columbia.

A new building is to be added to the Vancouver Tuberculosis Preventorium on its grounds, which are to be enlarged by some eleven acres to be leased from the City. Dr. W. H. Hatfield, so long active in tuberculosis in B.C., made the announcement lately.

This addition has become urgently necessary, to enable the Preventorium to handle its work properly. The Preventorium began operations in Vancouver some twenty years ago, and has done a magnificent job through the years. It was designed, as its name implies, not for active treatment, but for the housing and care of children who were contacts, or had been exposed. Educational facilities were provided, and adequate nursing care.

J. H. MACDERMOT

MANITOBA

The new wing of Flin Flon General Hospital was opened on January 27. It is three storeys in height and contains 42 beds and 17 bassinets. The hospital is operated by the Sisters of Charity of Hyacinth who also operate the hospital at The Pas. At the evening meeting the principle speaker was Judge J. M. George, president of the Associated Hospitals of Manitoba. Hon. Ivan Schultz, minister of Health and Public Welfare of Manitoba referred to Flin Flon as the gateway to the last Canadian frontier.

Dr. A. W. Andison and Dr. Ruvin Lyons of Winnipeg have been awarded the Fellowship of the Royal College of Obstetrics and Gynæcologists.

The Medical Health Officer of Winnipeg, Dr. Morley Lougheed, has recommended fluoridation of the water supply to provide one part per million. This recommendation was based on a dental examination of 17,568 school children from kindergarten to grade 6. Approximately 80% of the children were found to have decayed teeth. 14,000 children required immediate dental care, many very urgently. The survey was done with the assistance of a Federal Health grant and the voluntary assistance of over 80 Winnipeg dentists.

Dr. and Mrs. Comrie McCawley, recently of Bissett, Manitoba, left on February 20 for England where Dr. McCawley will take further postgraduate work in Obstetrics and Gynæcology.

A dinner was held in the Medical Arts Club rooms on February 29 by his friends in honour of Dr. F. G. McGuinness who recently retired as head of the Department of Obstetrics and Gynæcology, University of Manitoba.

ROSS MITCHELL

NEW BRUNSWICK

Dr. R. R. Prosser of the N.B. Department of Health discussed the mental health program of New Brunswick at the January meeting of the Saint John Medical Society. He outlined the planning of the Department including the training of key personnel and in general indicating the part that psychiatry should play in the community services.

The New Brunswick Society of X-Ray Technicians honoured the senior radiologists of the province at their last provincial meeting at Saint John. Honorary memberships were presented to Dr. H. L. Ripley, Dr. E. A. Petrie, Dr. W. A. Farrell and Dr. A. S. Kirkland.

At a joint meeting of the Washington County and St. Croix Medical Society held in St. Stephen, N.B., Dr. J. K. Sullivan spoke on "Genito Urinary Problems in General Practice". Dr. E. Stiles was chairman and the attendance was good.

Dr. J. A. Melanson, chief medical officer of the N.B. Department of Health was elected president of the newly formed N.B.-P.E.I. branch of the Canadian Public Health Association. The organization's meeting was held in Fredericton in February.

The Board of Trustees of the Miramichi Hospital at their February meeting reported receipt of gifts of hospital equipment for operating and x-ray departments from their generous benefactor Lord Beaverbrook.

Dr. Edward Weir, Dr. N. W. MacLellan and Dr. Lionel Guravich of the staff of D.V.A. Lancaster Hospital at Fairville, N.B., have been certified in Medicine by the Royal College of Physicians and Surgeons of Canada.

Under the postgraduate program of Dalhousie University, Dr. Fred W. Woolhouse of Montreal addressed the Moncton and district Medical Society on "Reconstructive Surgery of the Hand".

Dr. Henry Tonning has received his fellowship in medicine and Dr. Sidney Tobin his fellowship in Obstetrics and Gynæcology from the Royal College of Physicians and Surgeons. Both these doctors are on the staff of the Saint John General Hospital.

Dr. E. W. Ewart of Moncton on invitation presented a most interesting address to the Saint John Medical Society at their February meeting. He discussed the treatment of fractures and particularly some newer ideas in such treatment. He expressed the hope that the biologists and physiologists would shortly provide accurate information on the body processes that influence healing of fractures.

Dr. Don Sutherland and Dr. Eli Davis of the Saint John General Hospital staff were recently certified in Obstetrics and Gynæcology and Anæsthetics, respectively by the Royal College. Dr. Samuel Milrod was certified in Surgery.

A. S. KIRKLAND

NOVA SCOTIA

Dr. J. J. MacRitchie of the Provincial Department of Health had good words to say of the Nova Scotia hospitals in his annual report to Health Minister Connolly. Not a solitary complaint of hospital service has been received from the public at the department during the past year which, said Dr. MacRitchie, "should be an indication that the hospitals serve the people well". Commenting on Nova Scotia's nineteen county mental hospitals he reported that most of them are overcrowded and understaffed. Investigation showed care and treatment satisfactory but the situation is becoming very acute.

The City of Halifax has asked the province under the Federal Health Program to share part of the cost of a proposed four hundred bed mental hospital.

Dr. V. O. Mader, Halifax, was elected Commodore of the Royal Nova Scotia Yacht Squadron. Dr. Mader brings to this high post an experience of many years in the handling of small ships and racing craft off Nova Scotia's rocky coast.

Dr. J. S. Manchester has been given a new provincial grant to continue his postgraduate study in roentgenology after which he will return to the staff of the Victoria General Hospital.

Declaring that 10% of Canada's population is disabled or handicapped by mental illness or disturbances, Dr. J. D. M. Griffin, Director General of the Canadian Medical Health Association speaking in Yarmouth, made his contribution to the stimulation of a growing awareness among Nova Scotian profession and public of the need for development of mental disease treatment centres.

Dr. John Wickwire, Liverpool, was guest speaker in cardiology at the Dalhousie Postgraduate week in medicine.

Dr. W. I. Morse and Dr. R. E. Reid of Dalhousie Department of Medicine were guest speakers at the Annapolis Valley Medical Association meeting and at Yarmouth. Prior to the Annapolis meeting the members of the association were entertained at dinner by the Order of Good Cheer.

Dr. R. R. Prossor, Director of Mental Health Services for New Brunswick was a speaker at a two-day psychiatric seminar at Dalhousie University.

Despite a twenty-six man squad and a five platoon system of play the hockey team of the Victoria General Hospital visiting staff was decisively defeated by the intern-resident team in a thrilling match at the Dalhousie Memorial Rink. Donning skates with a do-or-die spirit the visiting team failed to show the superiority which they had hoped their years of medical training and experience would give them. In the nets Anæsthetist Kincaide showed again the coolness for which he is noted in crisis after crisis, and that the score was not more lopsided than 7-2 is largely to his credit. Another outstanding feature of the game was the defensive block of Neurosurgeon W. D. Stevenson. A return match is already planned and it is reported that the visiting staff are negotiating for the services of senior resident defenceman LeBrun who completes his resident term this year.

ARTHUR L. MURPHY

ONTARIO

The Toronto General Hospital campaign resulted in a total of $16,128,134, the largest sum ever raised for a hospital in Canada. The original objective was $14,000,000.

The federal government contributed one million, the city of Toronto three million, the Province of Ontario three million, the County of York $500,000, and the staff doctors $131,600.

Dr. Charles D. Stogdill has been appointed to fill a new post recently created, that of Director, Division of Mental Hygiene of the Board of Education, Toronto. Formerly mental hygiene work in the public schools had been carried on by a division of the city public health department but it was felt that the field was of sufficient importance and magnitude to warrant a full-time position within the Board of Education. Dr. Stogdill has been for a number of years Chief of the Division of Mental Hygiene in the Department of National Health and Welfare, Ottawa.

Dr. Arthur C. Singleton, acting director of the department of radiology, Toronto General Hospital and assistant professor of radiology, University of Toronto, has been elected chancellor of the American College of Radiology. He is a councillor of the Faculty of Radiologists, London and vice-president of the Canadian Association of Radiologists.

The Samaritan Club of Toronto gave assistance to 455 cases a month last year. About 35 new cases a month are cared for. Many of these are patients who have been discharged from sanitaria. Health Minister Phillips, in an address at the Samaritan Club annual meeting said that industry has an important place in the rehabilitation scheme, and should set aside a certain percentage of its jobs for sheltered employment of those persons who cannot go back to former occupations.

Last year the Ontario Division of the Canadian Cancer Society spent $69,000 on fellowships and grants-in-aid for research, $47,244 for service by furnishing cancer dressings and other comforts for cancer sufferers and $44,000 on an educational program to teach early detection by means of films, and literature.

Needy patients over 70 will continue to receive limited medical services through the Ontario Medical Association. The means test which will determine a pensioner's eligibility for this medical assistance will be the same as governs payment of the 65 to 69 pensions. The pensioner will be required to have an income, including pension, of not more than $720 a year if single, or $1,200 if married.

Dr. Angus Hood has been appointed executive director of the Mental Hygiene Consultation Services financed by the Community Chest of Greater Toronto. Dr. Hood, a graduate of Queen's, has been director of the Fort Wayne Child Guidance Centre, Fort Wayne, Indiana.

Dr. Martin Gumpert, New York, made two addresses in Toronto on Geriatrics. He said that the problems of retirement, of housing, of employability of the aged, of rehabilitation and retraining, of the rational use of leisure time, of family relationships between generations, of social security benefits, of emotional conflicts and mental hygiene and of adult education are closely connected with medical activities. He thinks that there is a need for geriatrics clinics and geriatric research.

There were 2,484 births at the Women's College Hospital in 1951 and not a single maternal death.

LILLIAN A. CHASE

PRINCE EDWARD ISLAND

Dr. F. A. McMillan recently returned from a week at the Montreal Urological Convention held January 7 to 12.

Dr. L. Prowse is at present in Washington, D.C. taking a course in the medical aspects of nuclear-energy at the United States Naval Hospital in Bethesda.

Dr. H. H. Pierce and Dr. E. S. Giddings are at present on tour with the Maritime Flying Curlers on their annual jaunt—this year to Detroit.

It has been decided to hold the Annual Convention this year at Prince of Wales College and we are expecting to have exhibitors for the first time at our Convention.

J. K. L. IRWIN

QUEBEC

Dr. Walter De M. Scriver, Associate Professor of Medicine, McGill University, left Montreal on February 27 to attend the British Commonwealth Medical Conference in Calcutta, India, on March 20 to 23, as representative of The Canadian Medical Association. Dr. Jessie Boyd Scriver accompanied her husband to the meeting as an official observer.

The idea of the British Commonwealth Medical Conference originated at a meeting of the British Medical and Canadian Medical Associations which was held in Montreal in 1906. The purpose is to provide a medium for a personal discussion, by specially appointed delegates, of professional problems of mutual interest.

The two doctors will fly around the world before returning to Montreal about May 1.

Plans are progressing for arrangements of the 19th International Physiological Congress, which will be held in Montreal from August 31 to September 4, 1953. Dr. C. H. Best of Toronto has been appointed President of this Congress. He was recently in Montreal meeting with the local committee, which consists of Drs. F. C. MacIntosh and G. Lyman Duff of McGill University, and Drs. Wilbrod Bonin and D. Marion of the University of Montreal.

The second Canadian Conference on Pædiatric Education, under the chairmanship of Dr. Alton Goldbloom, was recently held at McGill University and the Montreal Children's Memorial Hospital. The 2-day conference is sponsored by the Canadian Pædiatric Society and the American Academy of Pædiatrics. The purpose of these meetings is to study teaching problems with a view to raising and improving standards of teaching throughout the country.

The Mid-winter Clinical and Scientific Session of the Quebec Division of the Canadian Anæsthetists Society was recently held at St. Joseph's Hospital, Lachine, under the chairmanship of Dr. Wesley Bourne. The Clinical session was held in the morning and the scientific part of the meeting during the afternoon. The day's activities were concluded with a dinner at the El Paso Café.

Prof. Derek Denny-Brown recently delivered a memorial lecture for Dr. Donald McEachern at a meeting of the Montreal Neurological Society at the Montreal Neurological Institute. He spoke on "The Nature of Diseases of Muscle". In this he included considerable reference to papers by Dr. McEachern, together with some of his own observations. It is hoped that we will have an opportunity to publish this lecture in an early issue of the Journal.

The Annual Meeting of the Quebec Division will be held at North Hatley, Que., on Friday and Saturday, May 2 and 3.

Friday morning will be devoted to papers, the speakers and their subjects being: Dr. D. G. Cameron, Montreal, "Practical Considerations of the Rh Factor"; Dr. Guy Bertrand, Sherbrooke, "Practical Considerations of Abdominal Pain" (French); Dr. Jean Bouchard, Montreal, "Radiologic Evidences which may be secured in association with upper gastrointestinal hæmorrhage" (English); Dr. J. O'Neil, Sherbrooke, "Traitement des méningites" (French); Dr. J. C. Luke, Montreal, "Present status of the treatment of varicose veins" (English).

Dr. Rosaire Fontaine will be the luncheon speaker, and a panel discussion will follow on "The present day Nervous Woman".

The Annual Banquet in the evening will be addressed by the well-known author, Mr. Leslie Barnard, who will bring together such varied objects as "Writers, Books and Butterflies".

On Saturday the program will include the following papers: Dr. Eustace Morin, Quebec, "Recent Developments in the problem of removal of œdema fluid" (French); Dr. Angus D. McLachlin, London, Ont., "Surgery of the Diabetic Foot"; Dr. Raymond Simard, Montreal, "Abnormal Vaginal Bleeding" (French); Dr. Glenn Sawyer, St. Thomas, Ont., "The Modern Community Hospital".

The luncheon speaker will be Dr. D. P. Mowry of Montreal, who will speak on "Teeth and Food".

After lunch will come the well-known feature "Case Report for Diagnosis", when the usual guesses will be hazarded under the skilful guidance of Dr. G. Copping and J. Olivier.

The occasion has all the earmarks of a refreshing spring meeting.

SASKATCHEWAN

Dr. J. Wendell Macleod, Dean-elect of the Medical Faculty, University of Saskatchewan, is now on an extended tour of medical centres in the United Kingdom and Scandinavia. He will be returning to Saskatchewan toward the end of March. Dean W. S. Lindsay, who will be retiring in July, has been made an Honorary Member of the College of Physicians and Surgeons of Saskatchewan.

Dr. F. B. Roth has assumed the post of Deputy Minister of Public Health in Saskatchewan. Dr. Roth practiced at Whitehorse for some years after which he studied medical administration in Toronto. After a year in Winnipeg General Hospital on administrative duty he joined the Department of Public Health in Saskatchewan in 1950 as Director of the Department of Hospital Standards.

Dr. W. Storrar from England and Dr. G. W. Peacock from Ontario have joined the Department, the former as Director of Medical Services and the latter as Director of Hospital Standards.

Discussions have been completed between the Government of Saskatchewan and the College of Physicians and Surgeons to continue the operation of the Old Age Pensioners Medical Plan through the fiscal year 1952-3. A committee is being established between the Department and the College to study the plan and make

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recommendations to Government and Profession for the future operation of the plan.

Dr. H. Gordon Young, President of Council, announced on February 7, the resignation of the Registrar, Dr. Gordon Ferguson.

G. GORDON FERGUSON

GENERAL

A clearinghouse service on competent, ethical technicians specializing in braces, limbs, plastic eyes, or facial and body prostheses is being established. Qualified dentists doing obturator work or plastic eyes are included. Information will be available to all members of the medical profession on request. Everyone can assist this new service by forwarding names and addresses of qualified technicians and dentists to Academy-International of Medicine, 214 West Sixth St., Topeka, Kansas.

The federal government is this year contributing more than $25,000 toward the extension of mental health services at the Hospital for Sick Children, Toronto. The diagnostic service is available to children throughout Ontario, with cases being referred mainly from the Hospital for Sick Children's outpatient department, from private physicians, from community welfare agencies in the Greater Toronto area and from Children's Aid Societies throughout the province.

A psychiatrist gives short-term treatment, and a psychiatrist and a social worker provide intensive, long-term therapy for children in Toronto or its immediate district. A psychiatric treatment program for children in the hospital or in its convalescent branch at Thistletown has also been organized.

The federal grant provides for the part-time services of two psychologists who assist in the diagnostic program by carrying out psychometric tests and psychological appraisals.

Provision has also been made for three speech therapists who assist in the diagnosis of children's speech disorders. The diagnostic service is available to children from all parts of the province, and treatment can be given to those within commuting distance of the hospital.

1952 ESSAY CONTEST IN PLASTIC AND RECONSTRUCTIVE SURGERY.—The Foundation of The American Society of Plastic and Reconstructive Surgery offers awards in Junior and Senior classifications for original contributions in this field.

1. Junior classification.—Two 6-month scholarships in leading plastic surgery services in the United States, England and Italy. The contest is open to plastic surgeons in the specialty not longer than 5 years.

2. Senior classification.—Foundation's annual prize—Silver Plaque—for the best essay presented at the Annual Meeting of the A.S.P. & R.S.

The winning essays, in both classifications, will appear on the program of the forthcoming annual meeting of the A.S.P. & R.S. to be held in New York City, November, 1952. All entries must be received by the Award Committee not later than September 1, 1952. Further inquiries should be addressed to: The Award Committee, c/o Jacques W. Maliniac, M.D., 11 East 68th Street, New York 21, N.Y.

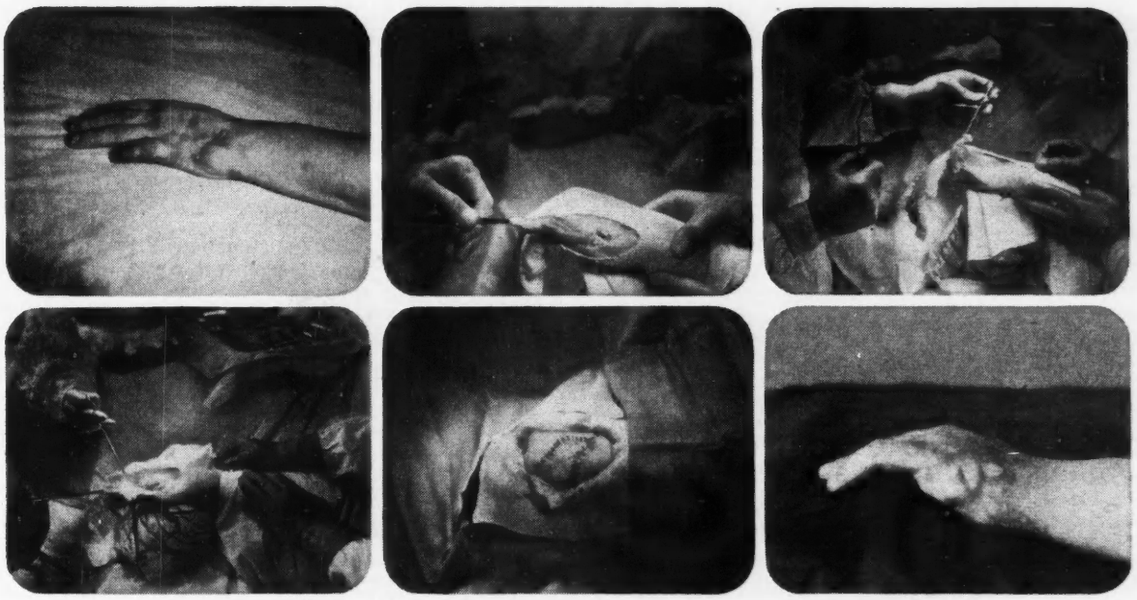
The following candidates were successful in the recent examinations of the Royal College of Physicians and Surgeons of Canada.

Division of Medicine.—Alway, A. E., London Ont.; Barnett, H. J. M., Toronto, Ont.; Bell, W. N., Philadelphia, Pa., U.S.A.; Berris, Barnet, Toronto, Ont.; Bocking, Douglas, Boston, Mass., U.S.A.; Boxall, E. A., Vancouver, B.C.; Brown, K. W. G., Toronto, Ont.; Cameron, C. G., Toronto, Ont.; Cameron, D. G., Montreal, Que.; Cronk, L. B., Belleville, Ont.; Darte, J. M. M., Toronto, Ont.: Delage, J. M., Quebec, Que.; Denton, R. L., Montreal, Que.; Finlayson, D. M., Toronto, Ont.; Fireman, H. H., Ottawa, Ont.; Frain, J. B., Philadelphia, Pa., U.S.A.; Gordon, R. A., Toronto, Ont.; Green, Norman, Toronto, Ont.; Holmes, R. B., Toronto, Ont.; Horlick, Louis, Montreal, Que.; Hudon, Fernando, Quebec, Que.; Jacques, André, Quebec, Que.; Kofman, Oscar, Toronto, Ont.; Little, J. A., Toronto, Ont.; Low, G. A., Toronto, Ont.; McBroom, G. L., Toronto, Ont.; Perry, A. W., Victoria, B.C.; Potvin, Laurent, Quebec, Que.; Prud'homme, Jean, Montreal, Que.; Reid, E. A. S., Montreal, Que.; Robinson, G. C., Vancouver, B.C.; Sanders, C. B., Toronto, Ont.; Spaulding, W. B., Toronto, Ont.; St-Pierre, Rosaire, Cap-de-la-Madeleine, Que.; Surchin, H. H. S., Montreal, Que.; Tonning, H. O., Fairville, N.B.; Vaisrub, Samuel, Winnipeg, Man.; Walters, M. B., Vancouver, B.C.; Wilson, D. L., Kingston, Ont.

Division of Surgery.—Allemang, W. H., Toronto, Ont.; Baker, C. B., Toronto, Ont.; Barber, H. O., Toronto, Ont.; Beaudet, J. A. H., Quebec, Que.; Boileau, G. R., Montreal, Que.; Blue, G. D., Toronto, Ont.; Brault, J. P., Montreal, Que.; Brown, W. A., Toronto, Ont.; Charest, Fernand, Verdum, Que.; Caudwell, G. G., Brantford, Ont.; Claman, A. D., Vancouver, B.C.; Clow, L. R., Kingston, Ont.; Coulonval, Louis, Quebec, Que.; Crimp, L. H., Toronto, Ont.; Culnan, G. F., Toronto, Ont.; Drake, C. G., Toronto, Ont.; Drouin, J. P.: Quebec, Que.; Duggan, J. W., Edmonton, Alta.; Ellenzweig, M. S., Hamilton, Ont.; Ernst, D. S., Kitchener, Ont.; Estranda, R. L., Montreal, Que.; Farish, J. R., Vancouver, B.C.; Ferguson, C. C., Boston, Mass., U.S.A.; Ford, H. S., Hamilton, Ont.; Ernst, D. S., Kitchener, Ont.; Estrada, W. D., Toronto, Ont.; Fulton, J. R. W., Toronto, Ont.; Funk, Henry, Winnipeg, Man.; Gaudry, Dominique, Chicoutimi, Que.; Gorman, T. W., Montreal, Que.; Gray, O. V., Toronto, Ont.; Greenway, R. E., Toronto, Ont.; Grundy, E. C., Toronto, Ont.; Isaac, J. E., Winnipeg, Man.; Karn, G. M., Montreal, Que.; Kozak, P. E., Montreal, Que.; Lafortune, Luc, Montreal, Que.; Lavers, G. D., Toronto, Ont.; Lloyd-Smith, W. C., Montreal, Que.; Lofthouse, R. N., Hamilton, Ont.; Marceau, Gilles, Quebec, Que.; Maughan, G. B., Montreal, Que.; Metcalfe, J. O., Edmonton, Alta.; Murray, J. F., Toronto, Ont.; Myers, E. D., Toronto, Ont.; MacCallum, E. A., Montreal, Que.; Macdonald, E. S., Toronto, Ont.; MacFarlane, K. T., Montreal, Que.; MacIntosh, R. A., Ville St-Laurent, Que.; McEwen, D. C., Iowa, Iowa, U.S.A.; McKenzie, A. D., Montreal, Que.; Niloff, P. H., Montreal, Que.; Orr, W. J., Toronto, Ont.; Osler, T. R., Vancouver, B.C.; Oxorn, Harry, Montreal, Que.; Peterson, C. L., Toronto, Ont.; Phaneuf, Jacques, Saint-Jean, Que.; Rees-Davies, P. E., Vancouver, B.C.; Ringuet, J.-J., Rimouski, Que.; Robertson, D. C., Toronto, Ont.; Routledge, J. H., Montreal, Que.; Saunders, G. M., Stellarton, N.S.; Smith, J. K. B., Toronto, Ont.; Speakman, T. J., Edmonton, Alta.; Spence, J. B., Toronto, Ont.; Stephens, C. A., Toronto, Ont.; Tardif, Guy, Edmundston, N.B.; Thompson, W. J., Vancouver, B.C.; Tobin, S. M., Saint John, N.B.; Townsend, R. G., Montreal, Que.; Watters, N. A., Toronto, Ont.; Wilson, B. M., Toronto, Ont.; Young, M. H. V., Montreal, Que.

A course in obstetrics for specialists in that field will be held at the Center for Continuation Study at the University of Minnesota on April 17 to 19, 1952. The visiting faculty member for the course will be Dr. S. R. M. Reynolds, Physiologist, Department of Embryology, Carnegie Institute of Washington, Baltimore, Maryland; and the remainder of the faculty of the course will be announced at a later date. Dr. Reynolds will deliver the annual Duluth Clinic Lecture on the subject of "Newer Concepts of Fetal Circulation", on Friday, April 18.

The four major American ear, nose and throat societies are meeting in the Royal York Hotel, Toronto with programs beginning on Sunday, May 18 and continuing until May 24. The following societies will be present: May



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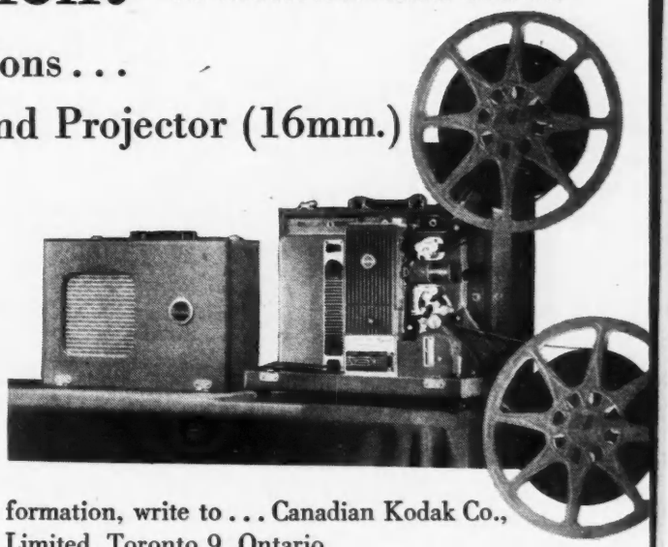

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18-19, American Otological Society. May 20 to 22, *Mornings*, American Laryngological, Rhinological and Otological Society. *Afternoons*, American Broncho-Esophagological Society. May 23-24, American Laryngological Society.

NEWS OF THE MEDICAL SERVICES

Canadian Armed Forces

Captain B. P. Doyle was recently appointed in the United Kingdom to a commission in the Canadian Army Active Force.

In accordance with the rotation policy for personnel serving in the Far East, Captains E. K. C. Fitzgerald, J. K. Besley and F. R. Cullen have returned to Canada after serving a tour of duty in Japan and Korea and Lieut.-Col. N. H. McNally, Major A. M. Davidson, Major B. D. Jaffey and Captain J. Y. Reid have been posted to the Far East as replacement medical officers.

Due to the urgent requirement of the Canadian medical commitment in Korea, it was necessary, a year ago, to interrupt the internships being served in civilian teaching hospitals by a number of recently graduated medical officers of the R.C.A.M.C. The Director General of Medical Services is now happy to announce that all of the officers thus affected are being returned to the hospitals which they left, to complete their internships. The names of the officers and the hospitals to which they will be going, are as shown: Captain J. A. Beswick, Toronto Western Hospital, Toronto, July 1, 1952; Captain W. R. Coleman, St. Michael's Hospital, Toronto, July 1, 1952; Captain E. K. C. Fitzgerald, St. Joseph's Hospital, Toronto, July 1, 1952; Captain D. S. Whittingham, Vancouver General Hospital, July 1, 1952; Captain W. E. Warwick, Royal Jubilee Hospital, Victoria, July 1, 1952; Captain J. K. Besley, St. Michael's Hospital, Toronto, July 1, 1952; Captain W. M. Crawford, Victoria Hospital, London, January 1, 53; Captain F. R. Cullen, Toronto Western Hospital, Toronto, January 1, 1953; Captain G. M. Marshall, St. Joseph's Hospital, Toronto, January 1, 1953.

Colonel M. H. Brown, O.B.E., R.C.A.M.C. (RF), Toronto, Consultant in Preventive Medicine to the Director General of Medical Services (Army), and Lieut.-Col. H. M. Stephen, C.D., R.C.A.M.C., Assistant Medical Director in charge of Preventive Medicine in the Directorate of Medical Services (Army), made a liaison visit to Japan and Korea in late February and early March to inspect the medical arrangements for the 25 Canadian Infantry Brigade Group.

Air Commodore A. A. G. Corbet, Director of Medical Services (Air) and a representative group of Medical Officers from the R.C.A.F. will attend the 23rd Annual Meeting of the Aero Medical Association in Washington, March 17 to 19, 1952. The R.C.A.F. will display a scientific exhibit and certain of the Medical Officers will be presenting scientific papers in the field of aviation medicine.

Flying Officer L. M. MacDonald, R.C.A.F. Nursing Sister; graduated from the last Para-Rescue Course. She is on the staff of the present course and gives instruction in first aid and physical training. She assists the Jump-master in the instruction of landing technique. Flying Officer MacDonald is the first female instructor in para-rescue training in Canada.

BOOK REVIEWS

THE CANADA YEAR BOOK 1951

The official statistical annual of the resources, history, institutions, and social and economic conditions of Canada. Published by Authority of The Right Honourable C. D. Howe, Minister of Trade and Commerce. 1219 pp., $3.00. King's Printer and Controller of Stationery, Ottawa, 1951.

The Canada Year Book manages most successfully to avoid the formal and sometimes even forbidding aspect of Government "blue books". Of course it has a great subject to deal with, but it is the handling of it that matters. Feature articles are available in reprint form and there is now a considerable volume of such material available. The present issue has among others special articles on Migratory Bird Protection, which points out the important international ramifications involved in the protection of bird life in Canada; Geology, with interesting diagrams and maps; Soil Zones; Forest Economy; and one on the Indians in Canada.

It is in the introduction however that one finds a general review of economic developments during the past year, and a linking together of them in relation to administrative policy. Reference is also made in a later chapter to expenditures on health grants, and other advances in public health and public medical care "to assist provincial health services and to prepare for a broad health insurance scheme". For a birdseye view of Federal and Provincial health activities, Chapter VII is invaluable.

The book is indispensable as an authoritative source of information about our country.

ROENTGEN ANATOMY

D. Steel, St. John's Hospital and Evangelical Deaconess Hospital, Cleveland, Ohio. 54 pp., illust. $9.50. Charles C. Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1951.

This volume consists of the standard views of the various body parts. The pictures are of good detail, with excellent lists of the various organ parts. For anyone who wishes to be able to interpret x-rays, this book is essential to provide the background of what is normal. The book is recommended to all those interested in the interpretation of x-ray films.

MANAGEMENT OF CŒLIAC DISEASE

S. V. Haas, Professor of Pædiatrics and Director of the Department, New York Polyclinic Medical School and Hospital and M. P. Haas. 188 pp. $5.00. J. B. Lippincott Company, Philadelphia, London and Montreal, 1951.

This new book presents a full history of cœliac disease in ancient as well as modern times. The authors discuss at some length the various etiological factors which have been proposed for this syndrome including endocrine disturbance, allergic background and possible psychological factors. The clinical picture and diagnosis are described and there is a considerable discussion of digestion and absorption. The relationship to fibrosis of the pancreas is referred to and speculation with regard to possible similar etiological basis. A valuable part of the book is a review of the methods of treatment and also of the prognosis. The author's own experience is a large one and the summary of his cases is very convincing. The simple dietary routine which is stressed should be helpful to those who find the disease difficult to treat. The author has long been known as an exponent of the use of ripe banana and the rationale for this is explained by him. The final chapter on an etiological hypothesis of the author's own is quite intriguing and also the extensive bibliography which is given.

THE KIDNEY

H. W. Smith, Professor of Physiology, New York University College of Medicine. 1049 pp., illust. $15.50. Oxford University Press, New York, 1951.

This monograph is a superb collection and integration of the presently available data regarding renal function. The text is, for the most part, lucid, definite, and authoritative; the author has made very important contributions in the field under discussion. All aspects of kidney function appear to have been included, the book being divided into four parts. Part I deals with the excretory mechanisms, as measured by clearances; Part II covers water and electrolyte balance and its control; Part III is concerned with circulatory and other factors affecting renal function; and Part IV considers the effects of both renal and extrarenal disease upon the kidney. The last lone chapter is on the diuretics.

Physically also, the book is pleasing, with good paper, type, and binding, and few errors. The illustrations are mostly diagrams and graphs; these are clear and well chosen to supplement the text. Their numbers are only just sufficient for this purpose; one must actually read this book, and not just look at the pictures. This is probably not a book for many medical practitioners; there is too much meat in it. But it certainly is a most convenient, if not absolutely indispensable, source of information for all those seriously concerned with renal physiology and the associated fields, and an excellent reference text for the undergraduate and graduate medical student.

THE PHARMACOLOGIC PRINCIPLES OF MEDICAL PRACTICE

J. C. Krantz, Jr. Professor of Pharmacology, School of Medicine, University of Maryland, Associate Professor of Pharmacology, School of Medicine, University of Maryland. 1116 pp., illust., 2nd ed., $11.25, Burns & MacEachern, Toronto, 1951.

Four reprints of the original edition of this book were required since its publication in 1949; this is mentioned as evidence of the demand there has been for it. This edition is similar to the first edition in purpose and plan, but extensive revisions and numerous additions have been made, so that it is considerably improved and very up-to-date. For example, ACTH and cortisone, aureomycin and terramycin, and radioactive iodine, are discussed.

The book undertakes to present the principles of the action of drugs as currently used in the treatment of disease, and it accomplishes this purpose very well. Sufficient physiology and biochemistry are introduced when necessary, to enable the reader to interpret the action of the drug under consideration in terms of these basic sciences; but the main purpose is never lost from view. It is well printed and bound. The illustrations are numerous and satisfactory; some are in colour. It was a real pleasure to review a book so nearly perfect, for the purpose for which it was intended, as this one is.

INHALATION ANÆSTHESIA

A. E. Guedel, Associate Clinical Professor of Surgery (Emeritus), University of Southern California School of Medicine. 143 pp., 2nd ed. $3.75. The Macmillan Company of Canada Ltd., Toronto, 1951.

The second edition of this work differs very little from the first in spite of a lapse of fourteen years between editions. The book is intended for beginners in anæsthesia and as such covers the basic principles and dangers common in inhalation anæsthesia.

Pentothal sodium and other short acting barbiturates which have become almost universal as inducing agents in the last fourteen years are not mentioned. Curare is mentioned but briefly. In view of the fact that so-called "balanced anæsthesia" with pentothal, curare and an inhalation agent are now so widely employed, and indeed taught to beginners, it is felt that this aspect of anæsthesia should have been discussed in some detail.